The effect of multimodal stimulation and cutaneous application of vegetable oils on neonatal development in preterm infants: a randomized controlled trial

L. Vaivre-Douret,* D. Oriot,† P. Blossier,‡ A. Py,† M. Kasolter-Péré‡ and J. Zwang§

*Univ Paris 10, Nanterre; Inserm, U669, Paris; Univ Paris-Sud and Univ Paris Descartes, UMR-S0669, Paris; AP-HP, Department of Child Psychiatry of Necker Hospital, Paris and AP-HP, Port Royal-Cochin Hospital, Department of Gynecology and Obstetrics, Paris
†Department of Neonatal and Pediatric Intensive Care, Universitary Hospital of Poitiers, Poitiers
‡Department of Child Psychiatry H. Laborit Hospital, Poitiers, and
§ISD – IRD, Institut Biomédical des Cordeliers, Univ Paris 6 (Pierre et Marie Curie), Paris, France

Accepted for publication 3 August 2008

Abstract

Background Preterm newborns admitted to the Neonatal Intensive Care Unit are deprived of sensory stimulation. Tactile/kinaesthetic stimulation results in weight gain. Studies involving the cutaneous application of vegetable oils have shown improvement in somatic growth and on skin barrier function.

Objective To assess the neurodevelopmental and biological benefits of the simultaneous use of multimodal stimulation (SMS) and the cutaneous application of vegetable oils.

Setting Tertiary referral centre serving the Poitou-Charentes region of France.

Methods Randomized controlled trial of 49 low-risk preterm infants, born at 31- to 34-week gestation. Each infant was randomly assigned to one of three treatment groups, Sensori-Tonico-Motor (STM) touch for 10 days with either: sweet almond oil, ISIO4 blended oil, or placebo – normal saline, or to a control group who did not receive any intervention. The primary outcome was weight gain. Secondary outcomes were linear growth, neurological maturation, psychomotor development and number of days of admission. Analysis was by intention-to-treat.

Results The group who received STM with ISIO4 oil demonstrated enhanced weight gain (+57%, 95% CI 37–76) compared with controls (P = 0.030). All STM groups showed shorter admission times (mean reduction 15 days, 95% CI 23–50 days hospitalised, P = 0.005), and an increase in body length (P = 0.030).

Both groups of oil massaged babies (almond and ISIO4) showed an increased neurological score (P = 0.001) compared to controls. The infants receiving ISIO4 oil had an associated increase in psychomotor scores (P = 0.028), time spent in quiet wakefulness (P = 0.036), improved orientation (P = 0.036), and enhanced development of the oculomotor (P = 0.012) and sensorimotor (P = 0.003) systems. An additional benefit seen was improved moisturization (P = 0.001), and quicker recovery of dermatological conditions. No adverse dermatological events were observed.

Conclusions The combination of STM and cutaneous application of oils to healthy preterm babies resulted in enhanced weight gain and neurological development, and a shorter stay in hospital.
**Introduction**

In the Neonatal Intensive Care Unit (NICU) the prevailing principle has been ‘minimal touch’ ever since a study by Long and colleagues (1980) showed that medical manipulations increased the risk of desaturations in preterm infants. However, several subsequent studies have indicated to the contrary (Morrow et al. 1991; Acolet et al. 1993). Paradoxically, the environment of the NICU overstimulates the preterm infant. This has encouraged care programmes to reduce their aggressiveness, as recommended in the Neonatal Individualized Developmental Care and Assessment Program (Als 1983), but this programme has been reported to be deficient in normal sensory experience (Field 1980). In utero, the foetus receives frequent tactile and vestibular stimulation through contact with the amniotic fluid and uterine wall, and these intrauterine sensations are necessary for normal growth and neurobehavioural development (White-Traut and Beth Carrier Goldman 1988; Mathai et al. 2001). After birth, the preterm infant will be deprived of these rudimentary stimulations.

Since the 1960s, different researchers have proposed various types of supplemental stimulation for hospitalized preterm infants with the aim of simulating the intrauterine environment in the first weeks of life, maintaining and facilitating the development of the preterm newborn (Mathai et al. 2001). The different programmes of stimulation have included combinations of tactile-kinesthetic and/or vestibular, auditory with visual stimulation but without all of these procedures being applied at the same time.

Despite methodological differences, the majority of studies including tactile and kinesthetic stimulation showed a benefit on weight gain of up to 53% supplementary gain (Field 2002). The average weight gain reported in the Cochrane meta-analysis was 5.1 g/day in comparison with controls (Vickers et al. 2005). Other observed effects were: earlier hospital discharge, by 3–6 days (Scafidi et al. 1990; Field 2002), progression from nasogastric tube feeding to oral feeding (White-Traut et al. 2002) and improved behavioural development in the neonatal period with accelerated maturation of the sleep-wakefulness system (Field 1980; Scafidi et al. 1993; White-Traut et al. 2002). These numerous benefits have been reported both in ‘healthy’ preterm infants and in newborns with different pathologies (Wheedeen et al. 1993; Field 2002; White-Traut et al. 2002). In all of these studies, there was no indication of whether a massage oil was used. However, some studies of newborn and preterm infants (Friedman et al. 1976; Hunt et al. 1978; Fernandez et al. 1987; Farrell et al. 1988; Lee et al. 1993) have demonstrated that the cutaneous application (massage) of vegetable oil could compensate for deficiencies of essential fatty acids (EFAs). A recent study showed (Soriano et al. 2000) better somatic growth of preterm infants massaged with soybean oil, while other researchers have observed a reduction in nosocomial infections with sunflower-seed oil massage (Darmstadt et al. 2005).

We conducted a study using the ‘Sensori-Tonico-Motor (STM) touch’ (Vaivre-Douret 1997, 2003) applying different vegetable oils (sweet almond, ISIO4) compared with a placebo (normal saline), and a control group (no intervention). The aims of the study were to assess the anthropometrical gain (weight, body length), neurodevelopmental, and potential somatic growth improvements resulting from simultaneous multimodal stimulation, and the biological benefits associated with application of different vegetable oils.

**Methods**

**Participants**

Between September 2002 and December 2004, we recruited preterm newborns admitted to the NICU at the University Hospital of Poitiers, France. Eligible infants were born at 31- to 34-week gestation, with no supplemental oxygen requirement, no congenital or genetic abnormalities, no Central Nervous System disturbances or maternal drug addiction, were randomly assigned to treatment groups. Newborn infants were excluded from the study if they required mechanical ventilation beyond 6 days of age, if the parents refused to enter/continue the study or if the infant was referred to another hospital.

The primary outcome on which the study was powered was weight gain. Based on a weight gain (SD) 25 (6) g/day in treated groups vs. 17 (6) g/day in control group (Field et al. 1986), and on 90% power to detect a significant difference 8 g/day ($P = 0.05$, two-sided), 15 subjects were required for each study group. The secondary outcomes for this study were linear growth, neurological maturation, psychomotor development and days of admission.

The study protocol was approved by the Consultative Committee for Human and Biomedical Research of Poitou-Charentes and by the ethics committee of the University Hospital of Poitiers. We obtained parental written consent for each infant recruited.

**Procedure**

After confirmation of eligibility by a neonatologist, the clinical researcher randomly assigned the preterm newborns, by a random number table, to the control group or one of three groups vs. 17 (6) g/day in control group (Field et al. 1986), and on 90% power to detect a significant difference 8 g/day ($P = 0.05$, two-sided), 15 subjects were required for each study group. The secondary outcomes for this study were linear growth, neurological maturation, psychomotor development and days of admission.

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treatment groups, in which the principal intervention was ‘STM touch’. Group C, the control group, received no ‘STM touch’ and no cutaneous treatment. The emollient applied on the skin to perform the ‘STM touch’ was a variant element with three different options: Group P (placebo) treated with application of normal saline; Group A with sweet almond oil (100%), a vegetable emollient (including 23.7% linoleic omega 6 and 0.2% linolenic omega 3 acids and 31 mg/100 g vitamin E) used traditionally in the practice of oil massage for newborn infants in France; group IS with the ISIO4 vegetable oil blend (Lesieur, France), consisting of four vegetable oils (52% sunflower, 25% high-oleic sunflower, 20% rapeseed, 3% grapeseed, including 42.1% linoleic omega-6, 1.9% linolenic omega-3 acids and 56 mg/100 g vitamin E).

‘STM touch’ was performed on the three treatment groups, for 15 min, twice per day during the periods of wakefulness at different moments from tube feeding or breastfeeding (morning and afternoon at 10:30 am and 3:00 pm) for 10 consecutive days. All subjects received standard nursing care throughout the course of the study. The length of the intervention period (from days 5 or 6 through days 15 or 16) was 10 days for all groups and was performed in the NICU in a room which had been specially equipped and heated.

Intervention

The specific method of ‘STM touch’ involved stimulating all sensory modalities (tactile, proprioceptive, vestibular, kinesthetic, auditory, visual and olfactory) simultaneously, not sequentially, in accordance with the Vaivre-Douret (1997, 2003) protocol. The newborn was placed on a warm Vestibulo® water mattress (vestibular modality) (Vaivre-Douret 2003) on top of a heated bed. The massage (tactile modality) consisted of a series of defined sequences designed to continuously stimulate all areas of the body with moderate pressure, moving from the abdomen to the thorax and shoulders, followed by one half of the body to cover the arm, hand and foot, and then the other half of the body and a ventral reversal to massage the back, shoulders and nape of the neck, ending with a dorsal reversal to touch the head and face. Thus, active changes in the position of the preterm infant were continuously provoked during the ‘STM touch’ (kinesthetic modality), guiding the preterm leg to obtain a co-ordination of the different limbs involved (head and trunk rotation, overpassing arm) with the reversal to lateral, ventral and dorsal decubitus positions. During the ‘STM touch’, the same soft music (Jean-Michel Jarre, France) was played (auditory modality). The psychomotor therapist (previously trained in ‘STM touch’) maintained continuous verbal contact (auditory modality) and eye contact (visual modality) with the newborn, under subdued lighting conditions. The newborns were not allowed to suck on a dummy during the ‘STM touch’. The quantity of oil (bottles stored away from light) or normal saline solution used for each infant is 5 mL, measured with a sterile syringe. Depending on the oil used, the olfactory modality was aroused to a greater or lesser extent. Only the therapist performing the ‘STM touch’ was aware of the group to which the newborn belonged; however, the therapist was blind to the hypotheses of the study. Neither the care staff nor the medical team had any knowledge of the treatment group to which the infant belonged.

Measures

Six types of variables were evaluated for each newborn, at approximately the same time period: length, weight and daily nutrition intake (calories, proteins, carbohydrates, fats and fluids) from birth until 21 days (end of the study). The weight of the naked newborn was measured every morning before bathing (if performed) using a Dina basic SP balance. The following variables (pre- and post-test study period) were evaluated at 5 or 6 days pre-intervention and at 15 or 16 days post-intervention respectively: biological variables, requiring a 2-mL sample of blood for long-chain fatty acids, insulin, glucose measurements.

Dermatological variables included a clinical evaluation of cutaneous status (softness of the skin, erythema, squamous skin, sclerotes), as well as a non-invasive measurement of the moisturization of each leg (on the external side of each thigh and the internal and external sides of each calf) by corneometry (CM825 PC, Cologne, Germany). This measures the electrical conductance which increases in proportion to the moisturization of the stratum corneum, the subject served as its own control (measurements between 6 and 8 pm after disinfection of the apparatus).

Neurological variables are measured according to the Amiel-Tison and Grenier (1986) examination. We calculated a neurological maturity score (Vaivre-Douret 1997, 2004; Vaivre-Douret et al. 2003) based on the level of maturity of following: oculomotor system, passive and active muscle tone of limbs, and primitive reflexes. A neuropsychomotor assessment protocol was performed (Vaivre-Douret 1997, 2003, 2004) using behaviour observation, of the duration of the quiet wakefulness state/duration during the examination, a neurosensorial examination with oculomotor tracking of a target and visual/auditory orientation of the examiner’s face and verbal stimulation, sensorimotor skills with spontaneous
organization of movements caused by the examiner. The physiological variables before and after the intervention period were measured by a scope from SpaceLabs Medical, Inc., USA: heart rate, respiratory rate, oxygen saturation (SpO₂) and body temperature measured in the armpit with a Digitalix 28 – thermofina thermometer. The care staff were responsible for recording the parental visit frequency, as well as the date of discharge.

The discharge decision was taken by the departmental doctors (unaware to which intervention group the child belonged), on the basis of: dietary status, gestational age, weight, weight gain, thermoregulation capability, haemodynamic and respiratory stability, and parental competence.

Throughout the study period, possible side effects were reported and the ‘STM touch’ protocol with the appropriate dose of oil or emollient was assessed by L.V.D. and M.A.K. prior to start the study and re-evaluated throughout the study period to ensure protocol compliance.

**Data analysis**

The stimulated groups (sweet almond, ISIO4, placebo), and controls were compared according to intention to treat principle analysis. Continuous data conforming to a normal distribution were compared using Student’s t-test and analysis of variance as appropriate. The categorical data were compared by calculating the chi-square value or by Fischer’s exact test. The data not conforming to a normal distribution were compared using the Mann–Whitney test, the Kruskall-Wallis, and the Wilcoxon signed rank test as needed. P-values were considered significant when \( P < 0.05 \). Data were analysed using spss for Windows version 14 (SPSS Inc.).

**Results**

Of the 60 eligible subjects (Fig. 1: CONSORT flow chart) there were seven consent refusals (refusal to take the necessary blood
sample at the start and end of the intervention), and four patients withdrew after the blood sample but before the stimulation intervention (two parental refusals and two transfers of infants to other hospitals for parental visit convenience). A total of 49 newborns were enrolled. Thirteen were allocated in a control group (C) and 12 in each group almond oil (A), ISIO4 (IS), and placebo (P). No adverse events or skin reactions were noted.

The baseline characteristics of the preterm newborns did not differ between the groups, except for birthweight and parenteral nutrition (Tables 1 and 2). There was no significant difference between the groups in relation to nutrition and formula intake or daily intake of proteins \((P = 0.999)\), carbohydrates \((P = 0.215)\), fats \((P = 0.283)\) and fluids \((P = 0.089)\).

**Weight gain**

Weight gain in the combined ‘STM touch’ groups was 30% higher than in controls, but this difference is not statistically significant \((P = 0.108)\). The significant increase in weight gain compared with the controls resulted from stimulation by massaging with the oil ISIO4 \((P = 0.030)\), with a weight gain in excess of +57% \((95\% \text{ CI 37–76})\). The preterm infants stimulated with the oil ISIO4 gained 301 g, 216 g in group A \(+13\%\), \(95\% \text{ CI 0–26}\), 230 g in the group P \(+20\%\), \(95\% \text{ CI 4–36}\), compared with 192 g in group C. Despite the weight difference at birth, the weight gain did not correlate with birthweight \((P = 0.231)\).

**Stimulation effects (‘STM touch’)**

The median length in days (range) of hospitalization of the newborns undergoing ‘STM touch’ \([26, (11–55)]\) was significantly shortened by \(-37\%\) \((95\% \text{ CI 23–50})\) compared with the controls \([41, (18–75), P = 0.005]\). This decrease of 15 days was an effect of the stimulation by ‘STM touch’, with the placebo group being discharged faster than the controls \((P = 0.022)\). The length of hospitalization was not related to the birthweight of the preterm infants \((P = 0.090)\).

After intervention, the body length of the stimulated preterm infants was significantly greater than in the controls \((P = 0.033)\); this resulted from the stimulation by ‘STM touch’ as placebos were also taller after intervention than the controls \((P = 0.030)\).

### Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sweet almond (A) ((n = 12))</th>
<th>ISIO4 (IS) ((n = 12))</th>
<th>Placebo (P) ((n = 12))</th>
<th>Control (C) ((n = 13))</th>
<th>Total ((n = 49))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(31 (63%))</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td>9</td>
<td>31 (63%)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>18 (37%)</td>
<td>0.747</td>
</tr>
<tr>
<td>Delivery</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td></td>
</tr>
<tr>
<td>Spontaneous vaginal</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>5</td>
<td>23 (47%)</td>
<td>0.472</td>
</tr>
<tr>
<td>Forceps delivery</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1 (2%)</td>
<td>0.369</td>
</tr>
<tr>
<td>Planned Caesarian</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>12 (24%)</td>
<td>0.381</td>
</tr>
<tr>
<td>Caesarian in emergency</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>13 (27%)</td>
<td>0.741</td>
</tr>
<tr>
<td>APGAR (mean)</td>
<td>(8.9)</td>
<td>(7.9)</td>
<td>(7.8)</td>
<td>(9)</td>
<td>(8.4)</td>
<td>0.317</td>
</tr>
<tr>
<td>1 min</td>
<td>(9.9)</td>
<td>(9.5)</td>
<td>(9.3)</td>
<td>(9.3)</td>
<td>(9.5)</td>
<td>0.428</td>
</tr>
<tr>
<td>Intensive care at birth</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>8</td>
<td>5</td>
<td>6</td>
<td>24 (49%)</td>
<td>0.436</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>25 (51%)</td>
<td></td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>(33.1 (0.8))</td>
<td>(33.5 (0.8))</td>
<td>(33.4 (0.9))</td>
<td>(32.7 (1.3))</td>
<td>(33.1 (1.0))</td>
<td>0.164</td>
</tr>
<tr>
<td>Hypotrophia</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td></td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>(1933 (297))</td>
<td>(1820 (397))</td>
<td>(1980 (283))</td>
<td>(1545 (335))</td>
<td>(1810 (364))</td>
<td>0.017</td>
</tr>
<tr>
<td>Birth length (cm)</td>
<td>(42.3 (3.2))</td>
<td>(41.7 (2.7))</td>
<td>(41.7 (1.9))</td>
<td>(40.3 (3.1))</td>
<td>(41.5 (2.8))</td>
<td>0.360</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>(30.5 (1.8))</td>
<td>(30.0 (1.7))</td>
<td>(30.4 (1.5))</td>
<td>(29.5 (1.8))</td>
<td>(30.1 (1.7))</td>
<td>0.562</td>
</tr>
<tr>
<td>Nutrition (number of days/21 days)</td>
<td>(15.2 (7.9))</td>
<td>(11.5 (8.6))</td>
<td>(12 (9.5))</td>
<td>(15.1 (6.1))</td>
<td>(13.5 (8))</td>
<td>0.547</td>
</tr>
<tr>
<td>Female or mother milk (F)</td>
<td>(4.2 (7.4))</td>
<td>(7.8 (8.9))</td>
<td>(6.5 (9.1))</td>
<td>(3.2 (5.3))</td>
<td>(5.4 (7.8))</td>
<td>0.536</td>
</tr>
<tr>
<td>Preterm milk formula (P)</td>
<td>(1.5 (2.8))</td>
<td>(2.2 (2.6))</td>
<td>(1.3 (2.5))</td>
<td>(2.7 (2.4))</td>
<td>(1.9 (2.6))</td>
<td>0.432</td>
</tr>
<tr>
<td>Mixed feeding (F + P)</td>
<td>(0)</td>
<td>(0)</td>
<td>(19 (-))</td>
<td>(0)</td>
<td>(19 (-))</td>
<td>-</td>
</tr>
<tr>
<td>Newborn milk formula</td>
<td>(0)</td>
<td>(0)</td>
<td>(19 (-))</td>
<td>(0)</td>
<td>(19 (-))</td>
<td>-</td>
</tr>
</tbody>
</table>

We indicated number \(n\) with the percentage or the mean and standard deviation in parentheses.
A similar pattern was observed for SpO2 in the stimulated groups with SpO2 increasing significantly after the ‘STM touch’ compared with the controls ($P=0.003$). The temperature of the stimulated groups was significantly lower after intervention ($P=0.002$) as well as the placebo compared with the controls ($P=0.002$). The heart rate was lower after the ‘STM touch’ ($P=0.012$) with no difference between groups A, IS, P ($P=0.856$), whereas it remained unchanged in group C ($P=0.929$).

**ISIO4 stimulation effects**

There was no pre-test difference in the groups neuropsychomotor characteristics. All groups showed neuropsychomotor progress during the study period, but the group IS showed a significantly higher total psychomotor score as compared with the controls and the placebos ($P=0.028$, $P=0.043$, respectively) (Table 3). The combined effect of the massage stimulation and the ISIO4 oil resulted in greater scores compared with the controls for the quiet wakefulness state. Oculomotor skills, visual-auditory orientation score, sensorimotor skills were significantly improved in the massaged groups compared with the controls, and improved in the group IS compared with the other oils groups ($P<0.05$ for all comparisons).

Skin conditions (e.g. eczema) were frequent in the preterm infants (30%, 14/47). The number of clinical dermatological pathologies decreased significantly in the ISIO4 group ($P=0.004$), but not in the group A ($P=0.097$), and was increased in the placebo group ($P=0.010$) compared with the controls. Thus, the dermatological improvement did not result from the stimulation alone ($P=0.422$) but from the ISIO4 oil.

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**Table 2.** Neonatal therapeutics and complications according to groups

<table>
<thead>
<tr>
<th>Control group (n = 13)</th>
<th>‘STM touch’ groups (A + IS + P) (n = 36)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonatal therapeutic practices (mean in days and SD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygenotherapy</td>
<td>0.5 (0.5)</td>
<td>0.5 (1.0)</td>
</tr>
<tr>
<td>Gavage</td>
<td>26.4 (13)</td>
<td>19.5 (7.7)</td>
</tr>
<tr>
<td>Glucose serum perfusion</td>
<td>6.6 (5.7)</td>
<td>6.0 (4.0)</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>6.5 (6.9)</td>
<td>1.6 (4.0)</td>
</tr>
<tr>
<td>Anti-biotherapy</td>
<td>4.4 (5.3)</td>
<td>2.7 (3.3)</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>0.4 (2.7)</td>
<td>3.9 (3.3)</td>
</tr>
<tr>
<td><strong>Medical complications (n, %)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>7 (54%)</td>
<td>20 (41%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3 (43%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Neurological</td>
<td>1 (14%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Anaemic</td>
<td>2 (29%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0 (0)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (14%)</td>
<td>3 (15%)</td>
</tr>
</tbody>
</table>

SD, standard deviation; groups: A, sweet almond oil; IS, ISIO4 oil; P, placebo; infections, perinatal bacterial infections; respiratory, instantaneous post-natal respiratory pathology; neurological, period intraventricular haemorrhage 1–3 gradients; anaemic, globulo transfusion; cardiac, arterial canal; others, digestive pathology, hypoglycaemia, alcoholic deprivation.

**Table 3.** $P$-value of comparison between ‘STM touch’ groups vs. control group in post-test period study of neurological and neuropsychomotor examinations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>‘STM touch’/C (A + IS + P/C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological maturity score</td>
<td>A/C 0.029</td>
<td>IS/C 0.001</td>
</tr>
<tr>
<td>Neuropsychomotricity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quiet wake state</td>
<td>0.409</td>
<td>0.036</td>
</tr>
<tr>
<td>Oculomotricity</td>
<td>0.225</td>
<td>0.016</td>
</tr>
<tr>
<td>Visual-auditory orientation</td>
<td>0.161</td>
<td>0.036</td>
</tr>
<tr>
<td>Sensory-motor skills</td>
<td>0.141</td>
<td>0.003</td>
</tr>
<tr>
<td>Total</td>
<td>0.119</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Groups: A, sweet almond oil; IS, ISIO4 oil; P, placebo; C, control.
Oils effects (almond, ISIO4)

The neurological maturation score by groups did not show any difference on admission ($P = 0.897$). All groups showed significant improvement in the post-test neurological score (Table 3). The total neurological score was significantly higher in the stimulated by oils groups ($P = 0.001$) compared with the control group, and there was no difference in the group P compared with the group C. The moisturization of the leg (thigh and calf) of the massaged preterm infants was significantly improved compared with the controls ($P = 0.009$). This was not related to the stimulation effect ($P = 0.369$), but to the effect of the oil ($P = 0.009$, $P = 0.002$, $P = 0.001$, for A, IS, and both, respectively).

Effect of the stimulation without oil

The higher increase in insulinaemia was in the group P compared with the control ($P = 0.048$), and IS ($P = 0.026$) groups was resulting from the stimulation without oil. We found no significant difference in glucose levels between the groups.

For the nine different fatty acids measured (C18:1, C18:2, C18:3n-3, C18:3n-6, C20:4n-6, C20:5n-3, C22:6n-3), we found no significant changes after intervention in any group. However, we observed significant differences in the post-test period: a reduction in C18:1 ($P = 0.022$) in group A and C20:4n-6 in groups P ($P = 0.005$) and C ($P = 0.017$), and an increase in C18:2 ($P = 0.028$) and C18:3n-6 ($P = 0.025$) in group P and C18:3n-6 ($P = 0.022$) in group C.

The frequency of daily parental visits to preterm infants receiving ‘STM touch’ (69%) was significantly higher than in controls (29%; $P = 0.005$). In group C, the visits were more often weekly (71%).

Discussion

This study showed the positive effects of ‘STM touch’ in French preterm newborns in relation to their body length ($P = 0.030$) and duration of hospitalization ($P = 0.005$) compared with the controls. For the group massaged with ISIO4 oil we observed greater weight gain, psychomotor scores, time spent in quiet wakefulness, improved orientation, and enhanced development of the oculomotor and sensorimotor systems, better moisturization, and recovery of skin conditions, as compared with the control group ($P < 0.040$ for all comparisons).

Infants in the control group had similar gestations but lower mean weight, length and head circumferences at birth. Thus, they were more growth restricted for their gestational age, as compared with the treatment groups; this could have affected the results of the study. However, there was no effect on weight gain as weight increase was not related to birthweight ($P = 0.231$). Another important bias that might have affected the results of our study was related to parental visit frequency. The parents of the controls visited much less than those of the intervention groups which could have affected the weight gain, neuropsychological scores and the behaviour (amount of quiet wakefulness) of the infants.

Using intention to treat as a principle for analysis provided an accurate assessment of the weight gain and insured an acceptable study validity although no patient withdrew from the clinical trial during the follow-up after the intervention.

Nevertheless, the infants receiving ‘STM touch’ showed a significant reduction in the length of hospitalization compared with the control group ($P = 0.022$) confirming results from the studies by Scafidi and colleagues (1990) and Field (2002), as well as the duration of parenteral feeding because of faster weight gain, as in White-Traut and colleagues (2002). Although the cost/effectiveness of this intervention was not assessed in this study, the reduction in hospital stay is likely to offset the cost of the therapist’s time.

The increased weight gain could also be explained by a higher caloric intake of the massaged groups. However, in our study as in majority of studies there was no significant difference in caloric intake between groups. The stimulation might therefore facilitate the transformation of the nutrients ingested into growth potential by accelerating anabolism (Field et al. 1986; Scafidi et al. 1990; Field 2002), and increase the vagal activity promoting the secretion of hormones involved in food absorption, in particular insulin (Field et al. 1987; Uvnäs-Moberg et al. 1987; Acolet et al. 1993; T. Field & S.M. Schanberg 1995, unpublished; Diego et al. 2005).

Our study showed a beneficial effect of moisturizing with vegetable oil, with better results for group IS than A that might be related to higher levels of vitamin E in this oil. However, the ability of EFAs to pass through the skin of preterm infants remains highly controversial (Friedman et al. 1976; Lee et al. 1993) as in the study by Lee and colleagues (1993) no significant difference was observed between the groups massaged with oil and controls. The quantity of oil applied on the skin in our study was likely to be insufficient, in relation to the body weight of the newborn, to detect a difference between almond oil and vegetable oils or to be detectable in the blood, there were no continuous readings of EFAs levels that indicate transient variations. Given the short period of exposure, the amount of oil used was small compared with the infants’ body weight which could be a possible limitation to this conclusion. The few
significant transcutaneous effect of the oils found in the blood has to be interpreted with caution as the changes could be confounded by other factors. Moreover, we could not assess or confirm how much of either oil crossed the skin/blood or blood/brain barrier. However, it has been shown that some oils might modify the skin barrier allowing a reduction in energy consumption (Fernandez et al. 1987; Nopper et al. 1996), and the multi-day application of vegetable oil might significantly improve somatic growth in preterm infants (Agarwal et al. 2000; Soriano et al. 2000). The changes observed in Fas might result from the physiological development of fat metabolism at different days of age, from the oil, the nasogastric feeding, the ‘STM touch’ intervention on the mobilization of the Fas or the potential transcutaneous passage of certain Fas, but the changes could also be due to other confounding factors.

Our study also showed that the ‘STM touch’ led to an increase in SpO2 and a decrease in heart rate, indicating a reduction in stress. It has been argued that massage may act on energy metabolism by reducing stress and pain in preterm infants (Acolet et al. 1993; Wheeden et al. 1993; Bellieni et al. 2002; Dieter et al. 2003). Respiratory rate was not affected by the ‘STM touch’, but we did not monitor it during the entire intervention procedure. Regarding temperature variations, some authors have noted a subtle reduction in temperature after massage within acceptable limits for preterm infants, and rapid recovery (White-Traut and Beth Carrier Goldman 1988; Acolet et al. 1993). Likewise, we observed a significant reduction in body temperature after massage indicating the effect of the ‘STM touch’.

Oils also had a significant impact on the progress of the neurological maturation score. The massaged groups, especially with ISIO4, showed better outcomes in neuropsychomotor wakefulness and in quiet wakefulness than in controls confirming the results of White-Traut and colleagues (2002). A possible limit to this conclusion was that the parents of the massaged groups visited their child more frequently than the parents of the control group which might strongly influence the baby's development. The significant increase in quiet wakefulness for the massaged groups could have long-term beneficial effects by promoting the bonding relationship and improving parent–child relationships associated with better capabilities at the cognitive level.

We suggest that the massaged groups might have achieved higher neurodevelopmental, neurosensory and motor performances associated with neuromotor stimulations provoked by the ‘STM touch’ with the activation of superior colliculus (McIlwain 1991). This might be responsible for the organization of visual saccades and plays an essential postural role in the support of the neck and head (tonus) and in body balance in association with the cortical pathways and somatosensory and auditory information with the reticular formation and cerebellum. The superior colliculus plays a crucial role thanks to its anatomical relationships in the context of multimodal stimulations facilitating cerebral plasticity by increasing the infant wakefulness.

This study was the first trial conducted in French preterm infants to show the benefits of simultaneous multimodal stimulation with vegetable oils, in particular ISIO4 oil, a rich source of EFAs. Massage with oil enhanced neurodevelopmental performance, improved the moisturization of the skin and reduced days in hospital. The implementation of a multimodal method of touch with ISIO4 oil to preterm infants has the potential to improve the quality of developmental care practice as well as the efficiency of the social public health system.

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**Key messages**

- This original randomized clinical trial presents the first study isolating the effects of intervention methods (with massage and/or vegetable oils) in French preterm infants.
- Massage with vegetable oils, in particular the oil ISIO4, a rich source of EFAs, led to a significant weight gain, a better neurodevelopmental performance, longer periods of quiet wakefulness, and an absence of cutaneous pathology indicative of good absorptivity and moisturization of the skin.
- The enhanced weight gain associated with simultaneous multimodal stimulation enabled an earlier discharge from hospital, with potential benefits for mother and child.

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**Acknowledgements**

We thank the families who participated in the trial, Dr S. Kayemba Kay's and Dr S. Besnier Dimaio for their general supervisior of the study’s data; the psychomotor therapists, E. Michaux, A. Le Pape and the Dr C. Catry for their clinical assessments; the Dermatology Department of Pr. G. Guillet for his clinical and technical assessment; Dr Cl Tallineau of the Bio-Chemistry Laboratory (Professor G. Mauco) and Dr C. Millet of the Nuclear Medicine Laboratory (Professor R. Perdrisot) for their technical skills in clinical biology and the staff and nurses of the NICU. We acknowledge the help
of Claudia Turner (Research Paediatrician, Shoklo Malaria Research Unit, SMRU) who reviewed the manuscript.

**Acknowledgements of support**

This study was supported by the Units 483 and 669 of National Institute of Health and Medical Research and by the Department of Child Psychiatry of Necker-Enfants Malades Hospital, Paris (Professor B. Golse), the Child Psychiatry Department of H. Laborot Hospital, Poitiers (Professor D. Marcelli), and the Necker Institute Research Fund, Paris through a grant from Lesieur Society, vegetable oil was provided by Lesieur Company, Paris.

The opinions expressed herein are those of the authors and do not necessarily represent the views of the sponsor who had no role in the study design, data collection, data analysis and data interpretation, or the writing of the final report.

**References**


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