

**Pre-feeding Sensorimotor Stimulation as an Early Intervention Strategy to
Enhance Oral Feeding Skills in Preterm Infants**

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In loving memory of my mother,

Francesca Ida Fucile,

her strength and courage

are my inspiration.

“There is no finer investment for any community than putting milk into babies.”

- Winston Churchill

ABSTRACT

Preterm infants are at high risk of encountering oral feeding difficulties. Safe and successful oral feeding entails the ability to coordinate suck, swallow, and respiration processes. Achievement of such coordination necessitates the function of multiple systems, including musculoskeletal, cardio-respiratory, gastrointestinal, behavioral, and neurological. Hence, oral feeding difficulties may ensue from oral and non-oral origins. There is limited knowledge on the effect of oral and non-oral intervention strategies aimed at optimizing oral feeding skills in preterm infants.

The objectives of this study was to investigate whether a pre-feeding uni-oral, uni-tactile/kinesthetic, and multi-oral+tactile/kinesthetic stimulation improve preterm infants' oral feeding skills, and to establish whether multi-sensorimotor interventions have an additive or synergistic effect leading to better oral feeding skills than uni-sensorimotor interventions.

Seventy-five preterm infants were randomly assigned to one of 4 groups: 1) uni-oral group, consisting of stroking the lips, cheeks, gums, tongue and sucking on a pacifier; 2) uni-tactile/kinesthetic group, involving stroking the body and limbs and passive range of motion to limbs; 3) multi-oral+tactile/kinesthetic group, consisting of oral and tactile/kinesthetic stimulation as above; and 4) control group.

All three experimental groups improved oral feeding performance, in particular time to attainment of independent oral feeding, proficiency and volume transfer, the uni-oral and multi-oral+tactile/kinesthetic groups increased rate of transfer, and the uni-oral group showed less volume loss (spillage) compared to controls. The underlying systems

mediating the oral feeding improvements differed for each intervention. The uni-oral stimulation enhanced nutritive sucking skills, suck-swallow-respiration coordination, and growth. The uni-tactile/kinesthetic stimulation improved suck-swallow-respiration coordination, growth, and motor function. The multi-oral+tactile kinesthetic stimulation increased suck-swallow-respiration coordination and motor function. The multi-oral+tactile/kinesthetic stimulation did not lead to additive or synergistic beneficial effects on oral feeding skills due to the shorter duration of each intervention.

Results support the concept that oral and non-oral sensorimotor stimulations are effective early intervention strategies to improve preterm infants' oral feeding skills, and bring to light the importance of both system specific sensorimotor input and duration of the input for improving defined outcomes. With this in-depth understanding of pre-feeding sensorimotor interventions it is essential to use them to their greatest advantage in neonatal care practices to benefit this vulnerable population of infants.

ABRÉGÉ

Les nourrissons nés avant terme ont souvent des difficultés pour se nourrir par voie orale. Une oralité sans risque nécessite la capacité de coordonner succion, déglutition et respiration. Ceci implique la participation des systèmes musculaire, cardio-respiratoire, gastro-intestinal, comportemental et neurologique. Les difficultés à s'alimenter par voie orale peuvent être d'origines orale et non-orale. Nous en savons peu sur les effets des interventions orales et non-orales visant à optimiser l'habileté du prématuré à l'oralité.

Les objectifs de cette étude étaient de déterminer si une intervention uni-orale, uni-tactile/kinesthésique ou multi-orale+tactile/kinesthésique offerte avant l'introduction de l'oralité peut améliorer l'habileté des nourrissons à s'alimenter par voie orale, et d'établir si une intervention multi-sensorimotrice a un effet additif ou synergétique sur l'oralité par rapport à une intervention uni-sensorimotrice.

Soixante-quinze nourrissons nés avant terme furent répartis de façon aléatoire en quatre groupes: 1) uni-oral, qui consiste à caresser les lèvres, les joues, les gencives et utiliser une suce; 2) uni-tactile/kinesthésique, qui implique les caresses du corps et des membres et un éventail de mouvements passifs aux membres; 3) multi-oral+tactile/kinesthésique, qui consiste en une stimulation orale et tactile/kinesthésique telle que décrite précédemment; et 4) contrôle.

Les trois groupes expérimentaux ont démontré de plus grandes habiletés pour l'alimentation par voie orale, en particulier du point de vue lapse de temps nécessaire pour transiter de l'alimentation par voie entérale à orale, de la compétence et du volume

transféré. Les groupes uni-oral et multi-oral+tactile/kinesthésique ont augmenté le rythme du transfert alors que le groupe uni-oral a démontré moins de perte de volume (déversement) que le groupe contrôle. Les mécanismes qui sous-tendent ces améliorations diffèrent d'une intervention à une autre. La stimulation uni-orale a amélioré l'habileté à la succion nutritive, la coordination succion-déglutition-respiration et la croissance. La stimulation uni-tactile/kinesthésique a amélioré la coordination succion-déglutition-respiration, la croissance et les fonctions motrices. La stimulation orale+tactile/kinesthésique a amélioré la coordination succion-déglutition-respiration et les fonctions motrices. La stimulation multi-orale+tactile/kinesthésique n'a pas mené à un effet additif ni synergétique bénéfique à cause de la plus courte durée de chaque intervention.

Les résultats soutiennent le concept que les stimulations sensorimotrices, orales et non-orales, sont deux interventions précoces efficaces pour améliorer l'habileté des nourrissons prématurés à l'oralité. Elles illustrent l'impact que l'apport sensorimoteur ainsi que la durée de cette stimulation peut avoir dans la maturation des fonctions oro-motrices. De telles interventions offertes avant l'introduction de l'oralité devraient être utilisées de façon avantageuse dans le cadre des soins néonataux pour soutenir cette population vulnérable.

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ABBREVIATIONS

BPD	Bronchopulmonary dysplasia
GA	Gestational age
E	Expiration
I	Inspiration
IVH	Intraventricular hemorrhage
NBRS	Nursery neurobiologic risk score
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NNS	Non-nutritive sucking
NS	Nutritive sucking
O	Oral
O+T/K	Oral plus tactile/kinesthetic
P	Pause
PMA	Postmenstrual age
PVL	Periventricular leukomalacia
Sk	Suck
Sw	Swallow
TIMP	Test of infant motor performance
T/K	Tactile/kinesthetic

GLOSSARY

Independent oral feeding: Ability to take all the prescribed volume of milk by mouth in eight oral feedings per day, within an allocated time.

Motor function: Defined by the following parameters: head and trunk control, postural alignment, and limb movement.

Oral feeding: Feedings taken by mouth through the process of suck-swallow-respiration, including both breast and bottle feeding.

Oral feeding performance: Defined by the following parameters: time to attainment of independent oral feeding, proficiency, volume transfer, rate of transfer and volume loss (spillage).

Oral feeding skills: Described by the following parameters: oral feeding performance, nutritive sucking, suck-swallow-respiration coordination, weight gain, and motor function.

PREFACE

The scope of research in neonatology is vast ranging from increasing the survival of the youngest and most medically fragile infants to optimizing their development. This thesis focuses on early intervention strategies to optimize the oral feeding skills of infants who are born prematurely. Up until now, little attention has been paid to reducing and/or preventing oral feeding difficulties in this high risk population as noted by the paucity of studies in this area of development. It is the author's opinion, that oral feeding is one of the most important developmental milestones for preterm infants to achieve because of its influence on their health, growth, development, quality of life, as well as family and social relations. This doctoral study was undertaken to examine the effect of pre-feeding sensorimotor interventions aimed at facilitating the acquisition of appropriate oral feeding skills in preterm infants. The work reported in this thesis was carried out between September 2002 and April 2008 at the School of Physical & Occupational Therapy, McGill University, QC, Canada and Texas Children's Hospital, an affiliate of Baylor College of Medicine, Houston, TX. It is hoped that this thesis provides the necessary evidence to highlight the importance of early interventions in this high risk group and represents a major step towards advancing further the field of neonatology and rehabilitaton science.

THESIS FORMAT

According to the guidelines set forth by the Faculty of Graduate Studies and Research, McGill University, the candidate has the option to submit a dissertation composed of one or more papers submitted or to be submitted for publication or the duplicate text of one or more published papers in the thesis. A manuscript-based format that contains four original papers has been selected as the format for the present thesis. The reader will note that repetition of some of the content will be found throughout the thesis because of the manuscript-based format.

The thesis comprises 8 chapters:

Chapter 1 is a general introduction and overview of this doctoral thesis.

Chapter 2 provides an in-depth review of the literature on oral feeding issues in preterm infants, which is presented in ten sections. The first section provides an overview of the incidence, definition, etiology, and significance of prematurity. The second section describes the oral feeding process, specifically sucking, swallowing, and respiration, and the coordination of these three functions. In section three, an oral feeding model that emphasizes the intrinsic neuro-physiological and extrinsic environmental factors involved in the oral feeding process is depicted. Section four summarizes the nature and causes of oral feeding difficulties. In section five, the current clinical management of neonatal oral feeding difficulties is explained. Section six outlines sensorimotor stimulation strategies providing an historical overview and theoretical framework. Sections seven and eight review the evidence on oral and tactile/kinesthetic sensorimotor stimulation, respectively, for maintaining and enhancing oral feeding skills. Section nine describes the multi-

sensorimotor stimulation approach to prevent or minimize oral feeding difficulties.

Section ten provides a summary and synthesis of the literature review.

Chapter 3 outlines the research rationale, which is followed by the objectives, specific aims, and hypotheses of this thesis. An overview of the research design is also provided.

Chapters 4, 5, 6, and 7 comprise four individual manuscripts investigating specific sensorimotor interventions and their beneficial effects on the oral feeding performance of preterm infants. Chapter 4 contains the first manuscript, “Pre-feeding sensorimotor interventions decrease the transition time to independent oral feeding in preterm infants,” which explores the impact of sensorimotor interventions, specifically uni-oral, uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations on preterm infants’ oral feeding performance. Chapter 5 contains the second manuscript, “Pre-feeding sensorimotor interventions promote nutritive sucking skills in preterm infants” which investigates the impact of uni-oral, uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations on preterm infants’ nutritive sucking skills. Chapter 6 contains the third manuscript, “Improvement of preterm infants’ suck-swallow-respiration coordination with pre-feeding sensorimotor interventions,” exploring the impact of the three sensorimotor interventions on suck-swallow and swallow-respiration coordination. Chapter 7 contains the fourth manuscript, “Sensorimotor stimulations improve growth and motor function in preterm infants,” which assesses the effect of each intervention on preterm infants’ growth i.e. weight gain, motor function, and length of hospitalization. These manuscripts will be submitted for publication in scientific peer-

reviewed journals. Preceding each manuscript are connecting texts which provide an integrative link between each of the manuscripts.

Chapter 8 provides an overall discussion of the main research findings highlighting original contributions, followed by a description of the clinical significance and implications of these findings along with study limitations, future research directions and a conclusion.

References are provided at the end of each chapter, and a full compilation of all references is included at the end of the thesis. Appendices are labeled by chapter number, followed by a letter, and are presented in order of the chapters.

CONTRIBUTION OF AUTHORS

The following are the four manuscripts included as part of this thesis and a description of the responsibility of each author:

Manuscript 1 Fucile S, Gisel E, Lau C. (2007) Pre-feeding sensorimotor interventions decrease the transition time to independent oral feeding in preterm infants.

To be submitted to: *The Journal of Pediatrics*.

Manuscript 2 Fucile S, Gisel E, Lau C. (2007) Pre-feeding sensorimotor interventions promote nutritive sucking skills in preterm infants. To be submitted to:

Developmental Medicine & Child Neurology.

Manuscript 3 Fucile S, Gisel E, McFarland D, Lau C. (2007) Improvement of preterm infants' suck-swallow-respiration coordination with pre-feeding sensorimotor interventions. To be submitted to: *Pediatric Research*.

Manuscript 4 Fucile S, Gisel E, Lau C. (2007) Sensorimotor stimulations improve growth and motor function in preterm infants. To be submitted to: *Early Human Development*.

The candidate is the primary author of the four manuscripts contained in this thesis, and claims responsibility for their style and content. The concepts of the research are the candidate's original work. The candidate was responsible for the planning and execution of the research in all four manuscripts, including writing of the research proposal for institutional scientific and ethical approval, recruitment of participants, administration of interventions, data collection, statistical analyses, interpretations of findings, and writing of the manuscripts. Statistical consultation was provided by Drs.

O'Brien Smith and Michal Abrahamowicz. The thesis committee is comprised of: Erika Gisel, Ph.D. (supervisor), Chantal Lau, Ph.D. (co-supervisor), and David McFarland, Ph.D. (expert advisor). The co-authorships of E. Gisel, C. Lau, and D. McFarland reflect their contribution to the manuscripts. For manuscript 1, 2, 3, and 4 these research papers proceeded under the direction of E. Gisel and C. Lau, thesis supervisors. For manuscript 3, D. McFarland provided expertise in the methods, data analyses, and interpretation of findings. All co-authors reviewed and provided feedback on the manuscripts.

STATEMENT OF AUTHORSHIP

I certify that I am the primary author of the manuscripts contained in this thesis. I claim full responsibility for the content of the text included herein.

TABLE OF CONTENTS

ABSTRACT.....	III
ABRÉGÉ.....	V
ACKNOWLEDGEMENTS	VII
ABBREVIATIONS	X
GLOSSARY.....	XI
PREFACE.....	XII
THESIS FORMAT	XIII
CONTRIBUTION OF AUTHORS	XVI
STATEMENT OF AUTHORSHIP	XVIII
LIST OF TABLES	XXIV
LIST OF FIGURES	XXV
CHAPTER 1.....	1
GENERAL INTRODUCTION.....	1
<i>1.1 References</i>	5
CHAPTER 2.....	8
LITERATURE REVIEW	8
<i>2.1 Prematurity</i>	8
<i>2.1.1 Incidence and definition</i>	8
<i>2.1.2 Etiology</i>	8
<i>2.1.3 Significance</i>	9
<i>2.2 Oral feeding process</i>	11
<i>2.2.1 Sucking</i>	11
<i>2.2.2 Swallowing</i>	13
<i>2.2.3 Respiration</i>	14
<i>2.2.4 Suck-swallow-respiration coordination</i>	15
<i>2.3 Oral feeding model</i>	19
<i>2.3.1 Intrinsic neuro-physiological factors</i>	19
<i>2.3.2 Extrinsic environmental factors</i>	22
<i>2.4 Oral feeding difficulties</i>	23
<i>2.4.1 Causes of oral feeding difficulties</i>	24
<i>2.5 Current clinical management of neonatal oral feeding</i>	27
<i>2.6 Early Intervention-Sensorimotor stimulation</i>	30
<i>2.6.1 Historical overview of practice approach</i>	31

2.6.2 Theoretical framework.....	32
2.7 Oral stimulation	36
2.7.1 Oral support.....	36
2.7.2 Non-nutritive sucking	37
2.7.3 Oral sensorimotor input.....	38
2.8 Tactile/kinesthetic stimulation.....	40
2.9 Multi-sensorimotor stimulation.....	41
2.10 Summary of literature review	43
2.11 References	45
 CHAPTER 3.....	 66
RATIONALE, OBJECTIVES, AND STUDY DESIGN	66
3.1 Rationale.....	66
3.2 Objectives.....	68
3.3 Hypotheses.....	68
3.4 Specific aims.....	69
3.5 Research design overview	70
3.6 References	75
 CHAPTER 4.....	 77
INTRODUCTION TO MANUSCRIPT 1.....	77
PRE-FEEDING SENSORIMOTOR INTERVENTIONS DECREASE THE TRANSITION TIME TO INDEPENDENT ORAL FEEDING IN PRETERM INFANTS.....	80
4.1 Abstract.....	81
4.2 Introduction.....	82
4.3 Methods	85
4.3.1 Participants.....	85
4.3.2 Interventions.....	86
4.3.3 Outcomes	87
4.3.4 Procedures	89
4.3.5 Statistical Analyses.....	91
4.4 Results.....	92
4.4.1 Participants.....	92
4.4.2 Oral feeding performance.....	92
4.4.3 Sensorimotor stimulations	94
4.5 Discussion.....	94
4.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions.....	94
4.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions	98
4.6 Conclusion.....	99

<i>4.7 Acknowledgements</i>	100
<i>4.8 References</i>	101
<i>4.9 Tables and figures</i>	107
 CHAPTER 5	 119
INTRODUCTION TO MANUSCRIPT 2	119
PRE-FEEDING SENSORIMOTOR INTERVENTIONS PROMOTE NUTRITIVE SUCKING SKILLS IN PRETERM INFANTS	 121
<i>5.1 Abstract</i>	122
<i>5.2 Introduction</i>	123
<i>5.3 Methods</i>	126
<i>5.3.1 Participants</i>	126
<i>5.3.2 Interventions</i>	127
<i>5.3.3 Outcomes</i>	128
<i>5.3.4 Instrumentation</i>	128
<i>5.3.5 Procedures</i>	129
<i>5.3.6 Statistical analyses</i>	131
<i>5.4 Results</i>	132
<i>5.4.1 Participants</i>	132
<i>5.4.2 Nutritive sucking skills</i>	132
<i>5.5 Discussion</i>	133
<i>5.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions</i>	134
<i>5.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions</i>	136
<i>5.5.3 Development of nutritive sucking skills</i>	136
<i>5.6 Conclusion</i>	137
<i>5.7 Acknowledgements</i>	138
<i>5.8 References</i>	139
<i>5.9 Tables and figures</i>	144
 CHAPTER 6	 153
INTRODUCTION TO MANUSCRIPT 3	153
IMPROVEMENT OF PRETERM INFANTS' SUCK-SWALLOW-RESPIRATION COORDINATION WITH PRE-FEEDING SENSORIMOTOR INTERVENTIONS	 155
<i>6.1 Abstract</i>	156
<i>6.2 Introduction</i>	157
<i>6.3 Methods</i>	163
<i>6.3.1 Participants</i>	163
<i>6.3.2 Study design</i>	163

6.3.3 Interventions.....	165
6.3.4 Outcomes	166
6.3.5 Instrumentation.....	168
6.3.6 Data reduction and statistical analyses	170
6.4 Results.....	171
6.4.1 Participants.....	171
6.4.2 Suck-swallow coordination.....	171
6.4.3 Swallow-respiration coordination	172
6.5 Discussion.....	172
6.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions.....	172
6.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions	174
6.5.3 Suck-swallow-respiration coordination	174
6.6 Conclusion.....	176
6.7 Acknowledgements.....	177
6.8 References	178
6.9 Tables and figure	184
 CHAPTER 7	 191
INTRODUCTION TO MANUSCRIPT 4.....	191
SENSORIMOTOR STIMULATIONS IMPROVE GROWTH AND MOTOR FUNCTION IN PRETERM INFANTS	 193
7.1 Abstract.....	194
7.2 Introduction.....	195
7.3 Methods	197
7.3.1 Participants.....	197
7.3.2 Interventions.....	198
7.3.3 Outcomes	199
7.3.4 Procedures	200
7.3.5 Analyses	202
7.4 Results.....	202
7.4.1 Participants.....	202
7.4.2 Weight gain	202
7.4.3 Motor function	202
7.4.4. Length of hospital stay.....	203
7.5 Discussion.....	203
7.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions.....	203
7.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions	206
7.5.3 Length of hospital stay.....	207
7.6 Conclusion.....	207
7.7 Acknowledgements.....	209
7.8 References	210
7.9 Tables and figure	216

CHAPTER 8.....	222
DISCUSSION	222
<i>8.1 Oral feeding performance.....</i>	<i>222</i>
<i>8.2 Nutritive sucking skills.....</i>	<i>225</i>
<i>8.3 Suck-swallow-respiration coordination</i>	<i>228</i>
<i>8.4 Growth and motor function</i>	<i>231</i>
<i>8.5 Length of hospital stay.....</i>	<i>235</i>
<i>8.6 Summary and synthesis of findings.....</i>	<i>236</i>
<i>8.7 Significance and clinical implications</i>	<i>238</i>
<i>8.8 Limitations.....</i>	<i>240</i>
<i>8.9 Future research directions</i>	<i>242</i>
<i>8.10 Conclusion.....</i>	<i>245</i>
<i>8.11 References</i>	<i>246</i>
 COMPILED LIST OF REFERENCES	 255
 APPENDICES	 i
Appendix 2A: Stages of sucking scale	ii
Appendix 2B: Oral feeding model	iii
Appendix 3A: Institutional review board approval.....	iv
Appendix 3B: Consent form	v
Appendix 3C: Uni-oral stimulation	viii
Appendix 3D: Uni-tactile/kinesthetic stimulation.....	ix
Appendix 3E: Multi-oral + tactile/kinesthetic stimulation	x
Appendix 3F: Control intervention	xi
Appendix 3G: Outcome variables	xii
Appendix 3H: Nipple bottle apparatus	xiii
Appendix 8A: Summary of findings.....	xiv
Appendix 8B: Oral feeding model & underlying systems.....	xv
Appendix 8C: System specific sensorimotor inputs.....	xvi

LIST OF TABLES

CHAPTER 4

Table 1:	Baseline characteristics of preterm infants in the 4 study groups.....	107
Table 2:	Covariate distribution between the 4 study groups.....	108
Table 3:	Number of days to make the transition to independent oral feeding	109
Table 4:	Features of the sensorimotor stimulations	110

CHAPTER 5

Table 1:	Participant characteristics	144
Table 2:	Covariates	145
Table 3:	Nutritive sucking outcomes at the three monitored oral feeding sessions..	146

CHAPTER 6

Table 1:	Participant baseline characteristics	184
Table 2:	Suck-swallow coordination outcomes at the three monitored oral feeding sessions	185
Table 3:	Mean percent occurrence of swallow-respiration patterns in the study groups at the three monitored oral feeding sessions	186

CHAPTER 7

Table 1:	Characteristics of preterm infants in the 4 study groups.....	216
Table 2:	Covariate distribution in the 4 study groups	217
Table 3:	Mean daily weight gain before, during, and after the sensorimotor interventions.....	218
Table 4:	Test of Infant Motor Performance Scores at the end of the sensorimotor intervention period	219

LIST OF FIGURES

CHAPTER 4

Figure 1:	Proficiency (%) at the three monitored oral feeding sessions.....	111
Figure 2:	Volume transfer (%) at the three monitored oral feeding sessions.....	113
Figure 3:	Rate of transfer (ml/min) at the three monitored oral feeding sessions.....	115
Figure 4:	Volume loss (ml) at the three monitored oral feeding sessions.....	117

CHAPTER 5

Figure 1:	Stages of sucking at the three monitored oral feeding sessions.....	147
Figure 2:	Suction amplitude at the three monitored oral feeding sessions.....	149
Figure 3:	Expression amplitude at the three monitored oral feeding sessions.	151

CHAPTER 6

Figure 1:	Swallow-respiration patterns.	187
Figure 2:	Sample tracing of swallow-respiration patterns.....	189

CHAPTER 7

Figure 1:	Test of Infant Motor Performance, percent distribution of typical and atypical motor behaviors at the end of the sensorimotor intervention period	220
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CHAPTER 1

GENERAL INTRODUCTION

Feeding disorders affect 25% of all children (Manikam & Perman, 2000).

However, infants born prematurely have a higher occurrence of feeding disorders than full term infants (Ross & Browne, 2002). It is estimated that 30 - 40% of preterm infants may encounter oral feeding problems (Hawdon, Beauregard, Slattery, & Kennedy, 2000; Rommel, De Meyer, Feenstra, & Veereman-Wauters, 2003). Oral feeding problems in the preterm population are a prominent public health concern because of their negative impact on children's health and quality of life (Hawdon et al., 2000; Manikam & Perman, 2000).

The modern era of neonatal care is characterized by significant technological advances in mechanical ventilation and the advent of medicinal therapies such as, exogenous surfactant and antenatal steroids (Crowley, Chalmers, & Keirse, 1990; Horbar, Wright, & Onstad, 1993; Stoelhorst et al., 2005). Such advances have dramatically increased the survival of the youngest and smallest preterm infants within the last three decades (Wilson-Costello, Friedman, Minich, Fanaroff, & Hack, 2005). From the 1980s to the present, the survival rate of preterm infants has risen by 29% (National Center for Health Statistics, 2004). This increase has resulted in approximately fifty thousand infants born prematurely each year in Canada and half a million in the United States (National Center for Health Statistics, 2004; Statistics Canada, 2004). Approximately 90% of infants born prematurely require highly specialized neonatal care (McGrath &

Braescu, 2004). Although such care saves lives, medical and developmental sequelae related to immaturity remain of concern (McGrath & Braescu, 2004).

One significant problem is preterm infants' ability to breast/bottle feed (Burklow, McGrath, & Kaul, 2002). The main issues and concerns related to oral feeding in this population are influenced by current health care policies (Kelly, 2006). Due to fiscal constraints, the neonatal intensive care units now aim for earlier hospital discharge of infants, to reunite families and to contain costs (Collins, Makrides, & McPhee, 2003; Kelly, 2006). The American Academy of Pediatrics (1998) proposed the following guidelines for discharge of preterm infants from the hospital: 1) ability to maintain stable cardio-respiratory function; 2) ability to maintain normal body temperature while in an open crib; and 3) ability to feed safely by mouth to ensure a sustained pattern of daily weight gain. As more infants are being sent home on apnea monitors and oxygen supplementation, oral feeding is often the remaining obstacle for discharge from the hospital (Schanler, Shulman, Lau, Smith, & Heitkemper, 1999). At present, the predominant clinical practice is to wait until preterm infants reach independent oral feeding before being sent home because of the lack of evidence supporting the benefits of discharging infants from the hospital on tube feeding (Collins et al., 2003).

The primary focus of care in the neonatal intensive care unit is on saving lives and preventing and/or minimizing the occurrence of severe medical complications (McGrath & Braescu, 2004). Very little attention is paid to safeguarding oral feeding skills. Rather, most practices use a rehabilitative approach, which focusses on remediation of oral feeding problems only after they become clinically significant (Bazyk, 1990; Premji, McNeil, & Scotland, 2004). However, neonatal oral feeding difficulties often delay

discharge from the hospital, negatively impact parent-infant bonding and they may lead to long-term feeding disorders causing growth failure (Burklow et al., 2002; Dodrill et al., 2004; Hawdon et al., 2000). Such consequences have enormous social and economic costs (Hawdon et al., 2000). A preventative approach can reduce and/or prevent the occurrence of neonatal oral feeding difficulties, and thus ease the burden of care. Hence, development of early intervention strategies are urgently needed to facilitate appropriate development of oral feeding skills in preterm infants (Burklow et al., 2002; Dodrill et al., 2004; Ross & Browne, 2002).

Oral feeding is contingent on the coordinated interaction of complex processes (Hill, 2002; Thoyre, 2003). These include sucking, swallowing and respiration, which are associated with the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral and neurological systems (Bu'Lock, Woolridge, & Baum, 1990; Burklow et al., 2002; McGrath & Braescu, 2004; Thoyre, 2003). Hence, oral feeding difficulties may arise from oral and non-oral origins. Pre-feeding sensorimotor intervention aimed at improving either oral or non-oral systems may enhance preterm infants' oral feeding skills. Furthermore, multi-sensorimotor interventions which focus on improving more than one system may have an additive or synergistic effect on oral feeding skills. Empirical evidence on the effects of pre-feeding oral and non-oral sensorimotor stimulation and the influence of uni- and multi-sensorimotor stimulations as early intervention strategies to enhance oral feeding skills in preterm infants is limited.

This prospective randomized clinical trial will examine the effect of three pre-feeding sensorimotor interventions on the oral feeding skills of preterm infants. Specifically, a uni-oral stimulation consisting of sensorimotor input to the cheeks, lips,

gums and tongue, a uni-tactile/kinesthetic stimulation involving sensorimotor input to the head, neck, trunk and limbs, and multi-sensorimotor stimulation consisting of oral plus tactile/kinesthetic stimulations, as described above, will be examined. In addition, the study will delineate the impact of uni- versus multi-sensorimotor interventions on oral feeding skills.

A more in-depth understanding of the impact of pre-feeding sensorimotor stimulations in this high risk population is essential to provide more efficacious interventions, to facilitate the acquisition of proper oral feeding skills and to minimize the occurrence of oral feeding difficulties, thereby promoting better long-term health and quality of life for children born prematurely and their families.

This doctoral thesis will proceed by reviewing the most current literature, describing the rationale for this study, outlining the objectives, hypotheses, specific aims, and providing a brief overview of the study design. The four manuscripts emanating from this thesis will follow, and a discussion synthesizing the main findings, clinical significance, study limitations, future research directions, and conclusion will be presented.

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CHAPTER 2

LITERATURE REVIEW

2.1 Prematurity

2.1.1 Incidence and definition

In Canada and in the United States, preterm births comprise 7.9% and 12.5% of all live births, respectively (National Center for Health Statistics, 2004; Statistics Canada, 2004). Prematurity may be defined by completed weeks of gestation or birth weight (World Health Organization, 1977). Accordingly, preterm birth refers to a birth that occurs before 37 completed weeks of gestation or a birth weight less than 2500 grams (World Health Organization, 1977). Further subdivisions to define prematurity have also been used in the recent literature, such as very and extremely preterm birth to describe an infant born less than 32 or 28 completed weeks of gestation, respectively. As well, very and extremely low birth weight is used to characterize infants weighing less than 1500 or 1000 grams at birth, respectively (Berkowitz & Papiernik, 1993; Caughy, 2006). Although both gestational age (GA) and birth weights are used to define cohorts of high risk infants, defining them on the basis of birth weight alone is less accurate because low birth weight can be the consequence of low GA, poor fetal growth, or both (Vincer et al., 2006). For this study, it is therefore preferable to define prematurity using the GA criterion.

2.1.2 Etiology

Preterm births are categorized as either spontaneous or indicated (Berkowitz & Papiernik, 1993; Caughy, 2006; Macones, 2005). Spontaneous preterm births, which

account for the majority of deliveries, occur because of preterm labor with intact membranes or premature rupture of the membrane (Berkowitz & Papiernik, 1993; Caughey, 2006; Macones, 2005). Indicated preterm births occur because of medical or obstetric problems (Berkowitz & Papiernik, 1993; Caughey, 2006; Macones, 2005). Several risk factors have been associated with both types of preterm births. These include, multiple gestations, history of spontaneous preterm birth, assisted reproduction, fetal abnormalities, uterine and cervical abnormalities, maternal infections, maternal age, i.e. adolescents and women 35 years of age or older, and low socioeconomic status defined on the basis of education, occupation, and family income (Berkowitz & Papiernik, 1993; Caughey, 2006; Macones, 2005).

2.1.3 Significance

Advances in perinatal and neonatal care have significantly reduced mortality due to preterm birth within the last 25 years (Emsley, Wardle, Sims, Chiswick, & D'Souza, 1998; Stoelhorst et al., 2005; Wilson-Costello, Friedman et al., 2005). However, neonatal morbidities in the surviving preterm infants remain a serious concern for public health officials (Emsley et al., 1998; Finnstrom et al., 1997; Stoelhorst et al., 2005; Wilson-Costello et al., 2005). Preterm birth is the leading cause of neonatal morbidity (Caughey, 2006). The occurrence of neonatal morbidity increases with decreasing GA (Hack & Fanaroff, 1999). Infants who are born prematurely are highly susceptible to nosocomial infections, necrotizing enterocolitis, retinopathy of prematurity, intraventricular hemorrhages, periventricular leukomalacia, and chronic lung disease (Chan et al., 2001; El-Metwally, Vohr, & Tucker, 2000; Finnstrom et al., 1997; Stoelhorst et al., 2005; Wilson-Costello et al., 2005). In addition to these medical conditions, they are also

vulnerable to oral feeding difficulties during the neonatal period (Bazyk, 1990; Harris, 1986; Hawdon et al., 2000).

Neonatal oral feeding difficulties in the short-term may affect growth, interfere with the transition from full tube to independent oral feeding, delay discharge from the hospital, and negatively affect the parent-infant bond (Bazyk, 1990; Burklow et al., 2002; Gardner & Hagedorn, 1991; Schanler, Shulman, & Lau, 1999). Furthermore, neonatal oral feeding difficulties put preterm infants at high risk for later developmental impairments (Hack & Fanaroff, 1999; Saigal, Burrows, Stoskopf, Rosenbaum, & Streiner, 2000). The long-term consequence of oral feeding difficulties include failure to transition to independent oral feeding necessitating prolonged and/or permanent tube feedings, altered oral sensitivity, facial defensiveness, inability to transition to solid foods, delays and/or aberrant oral-motor skills, as well as growth retardation and failure to thrive (Bazyk, 1990; Bier, Ferguson, Cho, Oh, & Vohr, 1993; Burklow et al., 2002; Comrie & Helm, 1997; Dodrill et al., 2004; Hawdon et al., 2000; VandenBerg, 1990). The implications of such long-term oral feeding problems are that they may interfere with children's health status and quality of life, intensify a maladaptive parent-infant relationship, and increase family psychological and emotional distress (Burklow et al., 2002; Hawdon et al., 2000). Such consequences are also associated with enormous financial costs (Hawdon et al., 2000; St. John, Nelson, Cliver, Bishnoi, & Goldenberg, 2000). To the author's knowledge, there are no data on the cost of caring for oral feeding disorders in this population. However, the total cost of care for the United States population of neonates is estimated to be over 10 billion dollars annually, with 57.3% spent on those born before 32 weeks of GA (St. John et al., 2000).

2.2 Oral feeding process

Safe and successful oral feeding is described as an infant's ability to take a prescribed volume of nutrient by mouth, within an appropriate amount of time, with no adverse reactions, including episodes of apnea, bradycardia and oxygen desaturation (Simpson, Schanler, & Lau, 2002). The oral feeding process involves the coordination of sucking, swallowing, and respiration (Bu'Lock et al., 1990; Goldfield, Richardson, Lee, & Margetts, 2006).

2.2.1 Sucking

Sucking is described as the rhythmic alternation of suction and/or expression components (Dubignon & Campbell, 1969; Lau, Alagurusamy, Schanler, Smith, & Shulman, 2000; Sameroff, 1968). Suction is the negative intra-oral pressure created by lowering the jaw and tongue (Colley & Creamer, 1958; Dubignon & Campbell, 1969). Expression is the stripping/compression of the nipple with the tongue against the hard palate (Ardran, Kemp, & Lind, 1958; Dubignon & Campbell, 1969). Sucking may be characterized as either non-nutritive or nutritive (Wolff, 1968). Non-nutritive sucking (NNS) is defined as sucking activity without the ingestion of milk (Wolff, 1968). Nutritive sucking (NS) involves the ingestion of milk, using either the expression component only or an alternation of suction and expression components (Lau, Sheena, Shulman, & Schanler, 1997; Wolff, 1968). The organization of a mature NNS pattern differs from a fully developed NS pattern in two factors: 1) NNS has a higher sucking rate (~2 sucks/second) than NS (~1 suck/second) (Dubignon & Campbell, 1969; Wolff, 1968), and 2) the NNS pattern is segmented into discrete sucking bursts and rest periods, whereas the NS pattern initially has a continuous sucking burst followed by intermittent

sucking bursts consisting of irregular bursts and longer rest periods (Jain, Sivieri, Abbasi, & Bhutani, 1987; Wolff, 1968).

Sucking activity appears in utero at about 15 weeks of fetal life (Ianniruberto & Taiani, 1981). Preterm infants are capable of displaying an organized NNS pattern as early as 30 weeks postmenstrual age (PMA, Hack, Estabrook, & Robertson, 1985). NS involves coordinated responses of swallowing the ingested milk and breathing which are not fully developed in younger preterm infants (Brake, Fifer, Alfasi, & Fleischman, 1988; Dubignon & Campbell, 1969). A mature NS pattern i.e. resembling that of a full term infant begins to be established at about 33-34 weeks PMA (Gewolb, Vice, Schwietzer-Kenney, Taciak, & Bosma, 2001). Specifically, infants less than 32 weeks gestation demonstrate a disorganized NS pattern that mostly consists of mouthing activity (Gewolb et al., 2001; Hack et al., 1985; Jain et al., 1987). This is followed by an immature NS pattern characterized by irregular sucking, consisting primarily of the expression component (Gewolb et al., 2001; Lau et al., 2000). A more mature NS pattern, similar to that of full term infants, is noted at about 33-34 weeks PMA, consisting of rhythmic alternation of both suction and expression components (Gewolb et al., 2001; Hack et al., 1985; Lau et al., 2000; Wolff, 1968). Lau et al. (2000) characterized the development of NS in infants born less than 30 weeks GA, by classifying their sucking pattern into 5 developmental stages, based on the presence/absence of the suction component, and on the rhythmicity and alternation of the suction and expression components (Appendix 2A). Stage 1, represents an immature/disorganized sucking pattern characterized by no suction, arrhythmic expression, and/or arrhythmic alternation of suction/expression. Stage 2, 3 and 4 represent maturing sucking patterns, with suction emerging, rhythmic

expression, and/or rhythmic alternation of suction and expression. Stage 5, represents a mature sucking pattern with a well defined rhythmic presence of suction and expression, similar to that of full term infants. Lau et al. (1997) found that a mature nutritive sucking pattern (stage 5) is not necessary to achieve safe and successful oral feeding in preterm infants. However, a significant positive correlation was found between stages of sucking and both overall milk intake and rate of milk transfer suggesting that the maturation of sucking skills plays a significant role in improving oral feeding performance (Lau et al., 2000).

2.2.2 Swallowing

Swallowing involves transporting the bolus of milk from the oral cavity to the esophagus (Arvedson & Lefton-Greif, 1998; Bosma, 1986). Swallow movements have been noted in fetuses as early as 13 weeks of gestation, indicating that the motor program for swallowing is functioning long before gestation is complete (Humphrey, 1967). Gewolb et al. (2001) found that a mature swallow rhythm, described as a stable peak-to-peak swallow interval, during oral feeding is established as early as 32 weeks PMA.

Swallow is conceptualized in the literature as having 3 distinct phases (oral, pharyngeal, and esophageal) or as a continuous process with an oropharyngeal phase and a subsequent esophageal phase (Bosma, 1986; Jean, 2001; Kramer, 1985). For this study, swallow will be described in three distinct phases because each phase can be clearly identified. During the oral phase, the bolus is formed and propelled into the region of the pharynx by front to back wavelike motions of the tongue (Arvedson & Lefton-Greif, 1998; Bosma, 1986, 1992). NS is considered the oral phase of swallow in infants (Arvedson & Lefton-Greif, 1998). During the pharyngeal phase, the soft palate rises and

the posterior pharyngeal wall constricts to close off the nasal airway (Arvedson & Lefton-Greif, 1998; Bosma, 1986, 1992). Further, the whole pharyngeal tube and larynx elevate, the epiglottis folds downward to cover the airway, and the true and false vocal cords contract to provide additional airway protection (Arvedson & Lefton-Greif, 1998; Bosma, 1986, 1992). The bolus moves through the pharynx by the combined action of pharyngeal peristalsis and changing pressure gradients within the pharynx (Arvedson & Lefton-Greif, 1998; Rudolph, 1994). During the esophageal phase the upper esophageal sphincter relaxes as the bolus enters the esophagus and is propelled to the stomach by peristaltic motion of the esophagus (Arvedson & Lefton-Greif, 1998; Rudolph, 1994). Despite the differences in conceptualization of swallow phases, there is a consensus that an effective swallow during oral feeding is one that prevents nasopharyngeal reflux (when milk flows back from the pharynx to the nasal passage), laryngeal penetration (when the bolus enters the larynx in the portion of the airway above the true vocal folds), and aspiration (when the bolus enters the airway below the true vocal folds before, during or after the pharyngeal phase of the swallow; Arvedson & Lefton-Greif, 1998; Jean, 2001).

2.2.3 Respiration

Respiration involves gas exchange to maintain a balance of oxygen and carbon dioxide in the blood in order to meet infants' changing metabolic needs, such as during oral feeding (Wolf & Glass, 1992). Respiration is always interrupted when a swallow occurs (McFarland, Lund, & Gagner, 1994; Wilson, Thach, Brouillette, & Abu-Osba, 1981). With an increase in the occurrence of swallows during oral feeding, there is a change in respiratory status (Mathew, 1991a; Shivpuri, Martin, Carlo, & Fanaroff, 1983).

Specifically, there is a marked decrease in minute ventilation and oxygenation, associated with a decrease in respiratory frequency, a reduction in inspiratory tidal volume, and a decrease in inspiratory time in full and preterm infants (Mathew, 1991a; Mathew, Clark, Pronske, Luna-Solarzano, & Peterson, 1985; Shivpuri et al., 1983). These changes are prominent during the initial continuous period of sucking (Mathew, 1991a; Shivpuri et al., 1983). Partial recovery of minute ventilation and oxygenation occurs during intermittent sucking (Mathew, 1991a; Shivpuri et al., 1983). The degree of subsequent recovery during intermittent sucking is positively correlated to PMA (Shivpuri et al., 1983). These respiratory changes during oral feeding may result in hypoxia, hypercarbia and acidosis which are manifested clinically as apnea, bradycardia and oxygen desaturation (Mathew, 1991a).

2.2.4 Suck-swallow-respiration coordination

Sucking, swallowing, and respiration individually are complex tasks, but during oral feeding, they must act together in a highly timed and coordinated manner to result in safe and efficient oral feeding (Goldfield et al., 2006). Specifically, the suck rate i.e. volume and speed of bolus formation will influence the frequency and timing of the swallow (Gewolb et al., 2001; Gryboski, 1969). Swallow as a protective mechanism suppresses respiration (Wilson et al., 1981). Therefore, the frequency and timing of swallow, in turn will affect respiratory rate and oxygenation (Wilson et al., 1981). All three processes must therefore be precisely coordinated so as to prevent and/or minimize any adverse events such as aspiration, choking, apnea, bradycardia, and oxygen desaturation (Arvedson & Lefton-Greif, 1998; Jean, 2001; Wolf & Glass, 1992).

Although our understanding is far from complete, it appears that establishment of suck-swallow-respiration coordination follows a gradual developmental progression (Bu'Lock et al., 1990; Gewolb & Vice, 2006; Gewolb et al., 2001; Holditch-Davis & Black, 2003; Lau, Smith, & Schanler, 2003). To the authors' knowledge, no systematic quantitative method has been developed to investigate suck-swallow-respiration coordination as one functional component. Rather the development of suck-swallow-respiration coordination has most commonly been studied as a function of suck-swallow and swallow-respiration, separately (Bamford, Taciak, & Gewolb, 1992; Gewolb & Vice, 2006; Gewolb et al., 2001; Mizuno & Ueda, 2003).

A coordinated suck-swallow pattern (i.e. a stable suck-swallow dyad) is achieved by 33-34 weeks PMA (Gewolb et al., 2001; Lau et al., 2003). Gewolb et al. (2001) noted that as development of sucking progresses, a stable suck-swallow dyad defined by peak-to-peak suck-swallow interval and ratio of number of sucks to swallows is also achieved. Specifically, in infants less than 33 weeks PMA, when mouthing movements or an irregular NS pattern is used, sucking is not consistently paired to swallow activity. However, at approximately 33-34 weeks PMA when a more mature NS pattern is used, sucking begins to be constantly linked with swallow (Gewolb et al., 2001). In support of this, Lau et al. (2003) demonstrated a 1:1 suck-swallow ratio is already achieved in preterm infants 33-34 weeks PMA during oral feeding.

Precise swallow-respiration coordination is vital for airway protection (Bamford et al., 1992; Gewolb & Vice, 2006; McFarland et al., 1994). The coordination of swallowing with respiration has been assessed by identifying the respiratory phase in which swallow occurs and further classifying the respiratory phases that precede and

follow the swallow (referred to as swallow-respiration pattern). The general goals of such analyses are to determine the overall stability of swallow-respiration coordination and its developmental time course (Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003). As well, the potential airway protective and other mechanical advantages of particular swallow-respiration patterns are assessed (Gewolb & Vice, 2006; McFarland et al., 1994; Mizuno & Ueda, 2003; Nixon, Charbonneau, Kermack, Brouillette, & McFarland, 2007). Although respiration is always inhibited to accommodate swallowing in all species, including infants and adult humans (Charbonneau, Lund, & McFarland, 2005; McFarland et al., 1994; Wilson et al., 1981), certain phase relationships (i.e. swallow-respiration patterns) may be safer and more efficient in particular air flow events that occur immediately before and after swallowing. In this regard, it has been suggested that swallows occurring within the expiratory phase or immediately preceded and followed by expiratory flow (i.e. expiration-swallow-expiration) are potentially the safest swallowing patterns in developing infants (Bamford et al., 1992; Gewolb & Vice, 2006; McFarland et al., 1994). In these cases, there is no inspiratory flow that could potentially bring residue into the open airway after the period of respiratory inhibition associated with swallowing (Gewolb & Vice, 2006). Swallowing in the expiratory phase also has potentially important mechanical advantages, such as facilitating laryngeal elevation and cricopharyngeal sphincter opening in both adults and infants (Charbonneau et al., 2005; McFarland et al., 1994; Nixon et al., 2007).

During non-nutritive swallow, the safest swallow-respiration pattern i.e. expiration-swallow-expiration has been noted in preterm infants at term corrected age (Nixon et al., 2007). However, during nutritive swallows this swallow-respiration pattern

is not achieved until beyond term age (Gewolb & Vice, 2006; Kelly, Huckabee, Jones, & Frampton, 2007; Lau et al., 2003; Miller & Kiatchoosakun, 2004). Several studies have demonstrated that swallow may occur at all phases of respiration during oral feeding in preterm and term infants (Bamford et al., 1992; Gewolb & Vice, 2006; Koenig, Davies, & Thach, 1990; Lau et al., 2003; Mizuno & Ueda, 2003). However, the predominant pattern, in preterm infants 34-35 weeks gestation, tended to be swallow during a prolonged respiratory pause, which was defined in these studies as cessation of breathing for greater than 2 seconds to accommodate swallow (Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003). This type of pause has previously been referred to as 'deglutition apnea' but should not be misinterpreted to be the same as the clinically significant conditions of apnea (Guilleminault, Li, Khramtsov, Palombini, & Pelayo, 2004; Miller & Martin, 1992). Lau et al. (2003) observed that the second most predominant pattern in preterm infants is swallowing during the inspiratory phase. This may explain the higher incidence of aspiration observed in preterm as compared with full term infants (Newman, Cleveland, Blickman, Hillman, & Jaramillo, 1991). With increasing age there is a decrease in swallows during prolonged respiratory pauses and an increased occurrence of swallows during the expiratory phase, suggesting an improvement in preterm infants' ability to breathe and feed orally at the same time (Gewolb & Vice, 2006; Kelly et al., 2007; Lau et al., 2003; Mizuno & Ueda, 2003). It is only past term that swallowing during the expiratory phase is fully attained (Bamford et al., 1992; Gewolb & Vice, 2006; Kelly et al., 2007; Lau et al., 2003; Selley, Ellis, Flack, & Brooks, 1990).

Taken together, suck-swallow-respiration coordination is critical for ensuring safe and successful oral feeding (Bu'Lock et al., 1990; Goldfield et al., 2006). Coordination of suck-swallow-respiration is a highly integrated multifaceted process (Goldfield et al., 2006). Safe and efficient suck-swallow-respiration coordination follows a gradual developmental course and is only achieved beyond term age (Gewolb & Vice, 2006; Gewolb et al., 2001; Lau et al., 2003; Mizuno & Ueda, 2003).

2.3 Oral feeding model

Oral feeding involves intrinsic neuro-physiological and extrinsic environmental factors (Burklow et al., 2002; Clark et al., 2003; Hill, 2002; McGrath & Braescu, 2004; Ross & Browne, 2002; Thoyre, 2003). The oral feeding model, proposed here, graphically depicts the interrelated nature of these factors enabling the oral feeding process (Appendix 2B).

2.3.1 Intrinsic neuro-physiological factors

The generation and coordination of suck-swallow-respiration necessitates the appropriate function and interaction of multiple systems, including the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral, as well as the neurological (Burklow et al., 2002; Hill, 2002; McGrath & Braescu, 2004; Miller & Kiatchoosakun, 2004; Ross & Browne, 2002; Thoyre, 2003). The *musculoskeletal system* refers to the anatomical structures, musculature, and postural control needed to generate suck, swallow, and respiration (Comrie & Helm, 1997; Shaker, 1990; Wolf & Glass, 1992). The anatomical structures include the nose, mouth, pharynx, larynx, trachea, esophagus, stomach, and lungs (Bosma, 1992; Kramer, 1985; Wolf & Glass, 1992). An extensive number of muscles are involved in generating sucking, swallowing, and respiration including those

of the cheeks, lips, tongue, pharynx and abdomen (Bosma, 1992). Correct postural alignment is important in the oral feeding process (Lemons & Lemons, 1996; Redstone & West, 2004). Alignment of the oral structures for sucking and swallowing is related to head stability, which is influenced by neck and trunk position (McFarland et al., 1994; Redstone & West, 2004). The physiological flexion position, as seen in full term infants, keeps the arms in midline, hips and knees flexed, head and neck flexed, and supports the rib cage and shoulder girdle. This position provides a stable base for sucking, swallowing and respiration (Bosma, 1973; Comrie & Helm, 1997; Shaker, 1990). The *cardio-respiratory system* involves the function of the heart and lungs to maintain adequate blood gas exchange of oxygen and carbon dioxide to meet infants' metabolic needs (Wolf & Glass, 1992). The mechanisms needed to maintain gas exchange include, change in respiratory rate, depth of respiration, and change in heart rate (Mathew, 1988, 1991b; Wolf & Glass, 1992). The *gastrointestinal system*, particularly upper and lower esophageal sphincter control, esophageal peristalsis, gastric emptying, and intestinal transport are needed for airway protection, adequate digestion and absorption of nutrients (Premji, 1998). The *behavioral system* is reflected in infants' level of alertness (McGrath & Braescu, 2004). The continuum stretches from a state of deep sleep to full arousal with crying (McGrath & Braescu, 2004). The quiet alert and active alert states are considered most optimal during oral feeding (Als, Duffy, & McAnulty, 1996; McCain, 1995, 1997; White-Traut, Berbaum, Lessen, McFarlin, & Cardenas, 2005).

The function and interaction of these multiple systems is dependent on the degree of maturity of the *neurological system* (Miller & Kiatchoosakun, 2004). At the level of the peripheral nervous system, the oral, nasal, pharyngeal, laryngeal, and tracheal

structures are primarily innervated by motor and sensory branches of the cranial nerves V, VII, IX, X, XII and branches of the upper cervical roots of C1-C5 (Jean, 2001; Miller & Kiatchoosakun, 2004; Wolf & Glass, 1992). The neck, shoulder girdle, heart, lungs, and digestive structures are also innervated by the upper cervical roots and cranial nerve X (vagus nerve) (Jean, 2001; Miller & Kiatchoosakun, 2004; Wolf & Glass, 1992). At the level of the central nervous system, the neurological functions of respiration, digestion, heart rate, and arousal (behavioral state) are located in the brainstem (Jean, 2001; Miller & Kiatchoosakun, 2004). The brainstem, particularly the pons and medulla, is also the region essential to the basic responses of suck-swallow-respiration (Jean, 2001; Miller & Kiatchoosakun, 2004). Most afferent inputs of suck, swallow and respiration are received in the nucleus of the tractus solitarius, and the efferent controls are mainly localized in the nucleus ambiguus (Jean, 2001; Miller & Kiatchoosakun, 2004; Wolf & Glass, 1992).

The considerable overlap in peripheral and central neural control forms the basis for reciprocal influences of suck-swallow-respiration (Wolf & Glass, 1992). Moreover, it is theorized that the rhythm of suck, swallow and respiration is generated within the brainstem (pons and medulla) by neural circuits called central pattern generators (Barlow & Estep, 2006; Finan & Barlow, 1998; Jean, 2001; Lund & Kolta, 2006; Miller & Kiatchoosakun, 2004). The central pattern generators are conceptualized as flexible organized neural networks with multifunctional nerves producing specific motor behaviors (Barlow & Estep, 2006; McFarland & Tremblay, 2006). It is postulated that central pattern generators not only function to coordinate activity within the sucking, swallowing and respiration systems, but also the tight neural coordination between these three processes (Barlow & Estep, 2006; McFarland & Tremblay, 2006). The integration

of afferent sensory feedback into the central pattern generators allows the systems to adapt rapidly to external perturbations in the oral, pharyngeal, laryngeal and respiratory areas (Finan & Barlow, 1998; Jean, 2001; Lund & Kolta, 2006; Miller & Kiatchoosakun, 2004). Therefore, mature and intact sensory and motor neural connections are needed to establish and maintain suck-swallow-respiration coordination (Barlow & Estep, 2006; Finan & Barlow, 1998; Jean, 2001).

2.3.2 Extrinsic environmental factors

Extrinsic environmental factors which may also affect the oral feeding process include the caregiver, the physical surrounding, and the equipment (Lemons & Lemons, 1996; McGrath & Braescu, 2004; Thoyre, 2003). Research conducted on the *caregiver* role in feeding demonstrates that infants' feeding skills may be enhanced through appropriate caregiver support (Als et al., 1996; Thoyre, 2003). Sensitivity to infants' responses during feeding, co-regulation of feeding (e.g. pacing the feeding), and reciprocity, which is defined as an ability of both the caregiver and infant to adjust appropriately to each others' cues during the feeding, play a role in this interaction (Als et al., 1996; Thoyre, 2003). The literature in the area of environmental factors indicates that the *physical surrounding*, such as the noise level, light intensity, and ambient temperature can influence oral feeding performance by causing distractions and undue distress to infants (Als et al., 1996; Catlett & Holditch-Davis, 1990). There is strong evidence demonstrating that the characteristics of the *equipment* used to feed the infant, in particular the size of the nipple hole, the type of bottle (i.e. standard bottle or vacuum-free bottle), and the consistency and taste of the nutrient received (i.e. breast milk, formula, or glucose water) affect infants' sucking, swallowing, and respiration

coordination during oral feeding (Bamford et al., 1992; Crook & Lipsitt, 1976; Duara, 1989; Goldfield et al., 2006; Lau & Schanler, 2000; Mathew, 1990; Mizuno, Ueda, & Takeuchi, 2002; Scheel, Schanler, & Lau, 2005).

According to this oral feeding model, safe and successful oral feeding is achieved when infants are able to maintain a balance between intrinsic neuro-physiological and extrinsic environmental factors with no adverse events. The majority of healthy full term infants are able to safely and successfully coordinate suck-swallow-respiration processes within a few hours of birth (McGrath & Braescu, 2004; Miller & Kiatchoosakun, 2004; Weber, Woolridge, & Baum, 1986). However, attainment of safe and successful oral feeding in preterm infants is a gradual developmental process dependent on the proper maturation, function, and interaction of intrinsic neuro-physiological factors and well-matched extrinsic environmental factors (Burklow et al., 2002; Hill, 2002; McGrath & Braescu, 2004; Pickler, 2004; Ross & Browne, 2002; Thoyre, 2003).

2.4 Oral feeding difficulties

Preterm infants may experience numerous forms of oral feeding difficulties; however, only the most commonly encountered problems will be outlined. With respect to sucking difficulties, preterm infants often present with trouble latching onto the nipple, poor lip seal, decreased tongue cupping, disorganized sucking pattern, and difficulty maintaining a rhythmic sucking pattern (Burklow et al., 2002; Comrie & Helm, 1997; Hawdon et al., 2000; McGrath & Braescu, 2004; VandenBerg, 1990). In terms of swallowing difficulties, preterm infants may have a delayed or poorly coordinated swallow response, nasopharyngeal reflux, laryngeal penetration, and aspiration. These may present clinically as coughing, gagging, and choking during oral feeding (Bazyk,

1990; Comrie & Helm, 1997; Lemons & Lemons, 1996; Mathew, 1991b; VandenBerg, 1990; Vogel, 1986). With regard to respiration difficulties, preterm infants have difficulty maintaining adequate respiration, leading to episodes of apnea, bradycardia, and oxygen desaturation (Comrie & Helm, 1997; Mathew, 1988, 1991a, 1991b; Thoyre, 2003). Any of the above sucking, swallowing and respiratory difficulties, may lead to poor suck-swallow-respiration coordination (Comrie & Helm, 1997; Mathew, 1991b; Thoyre, 2003; VandenBerg, 1990). Furthermore, it takes energy to do the work of sucking, swallowing and respiration (VandenBerg, 1990). Preterm infants are weak and fatigue easily (McGrath & Braescu, 2004; VandenBerg, 1990). Fatigue becomes a problem when they tire before they have taken a sufficient volume of milk, or if they become medically compromised by apnea, bradycardia, or oxygen desaturation during oral feeding (Comrie & Helm, 1997; Thoyre, 2003; VandenBerg, 1990). Preterm infants may also present with oral hypersensitivity or aversion which is manifested by avoidance behaviors, such as turning the head away, crying, and gagging upon oral or facial stimulation (Bazyk, 1990; Dodrill et al., 2004; Harris, 1986; VandenBerg, 1990).

2.4.1 Causes of oral feeding difficulties

Oral feeding difficulties encountered in this population can be due to intrinsic neuro-physiological factors, extrinsic environmental factors, or a combination of the two (Burklow et al., 2002; Gardner & Hagedorn, 1991).

Intrinsic neuro-physiological factors contributing to oral feeding difficulties include immaturity and neonatal morbidities. Immaturity of the musculoskeletal, gastrointestinal, behavioral, and neurological systems all contribute to difficulty with oral feeding (Burklow et al., 2002; Comrie & Helm, 1997; Gardner & Hagedorn, 1991;

VandenBerg, 1990). Specifically, infants who are born prematurely have underdeveloped oral and pharyngeal musculature, and general hypotonia leading, for instance, to difficulty latching onto the nipple, poor lip seal, and a disorganized sucking pattern (Comrie & Helm, 1997; Gardner & Hagedorn, 1991; VandenBerg, 1990). Moreover, because of their hypotonia they may not be able to maintain the flexor posture needed for safe sucking, swallowing and respiration (Burklow et al., 2002; Gardner & Hagedorn, 1991; Shaker, 1990). Preterm infants may be unable to meet their respiratory needs during oral feeding due to immature cardio-respiratory function, resulting in adverse events, such as apnea, bradycardia, and oxygen desaturation (Burklow et al., 2002; Mathew, 1988, 1991a). Gastrointestinal motility and gastric emptying are less well developed, predisposing preterm infants to feeding intolerance, abdominal distention, aspiration and vomiting (Burklow et al., 2002; Neal, 1995; Premji, 1998). Preterm infants may be unable to sustain the optimal behavioral states i.e. quiet or active alert states for prolonged periods of time, which in turn negatively impact their oral feeding performance (Comrie & Helm, 1997; Pickler, 2004).

Preterm infants are highly vulnerable to serious neonatal morbidities affecting their oral feeding skills (Burklow et al., 2002). These include morbidities of the cardio-respiratory system, particularly respiratory distress syndrome and bronchopulmonary dysplasia; morbidities of the gastrointestinal system, most commonly gastroesophageal reflux disease and necrotizing enterocolitis; as well as insults to the neurological system, such as intraventricular hemorrhages and periventricular leukomalacia (Bazyk, 1990; Gardner & Hagedorn, 1991; Gewolb, Bosma, Reynolds, & Vice, 2003; Neal, 1995). These neonatal morbidities may interfere with infants' ability to attain sucking,

swallowing and respiration and/or decrease their tolerance to oral feeding (Bazyk, 1990; Gardner & Hagedorn, 1991; Gewolb et al., 2003; Neal, 1995).

Extrinsic environmental factors contributing to oral feeding difficulties include medical interventions and the physical surrounding. Many medical interventions responsible for preterm infants' survival inhibit important sensorimotor experiences and expose them to noxious oral stimuli which may impair the establishment of appropriate oral feeding skills (Burklow et al., 2002). For instance, prolonged tube feedings (orogastric and nasogastric) for nutritional support prevent infants from experiencing positive oral input from feedings, and it may also impinge on pharyngeal, laryngeal and esophageal spaces causing discomfort during swallowing (Arens & Reichman, 1992; Dodrill et al., 2004; Harris, 1986; Shiao, Youngblut, Anderson, DiFiore, & Martin, 1995). Prolonged endotracheal intubation can cause subglottic stenosis, palatal groove formation or acquired cleft palate, resulting in disorganized suck-swallow coordination (Bier et al., 1993; Comrie & Helm, 1997). Furthermore, these aforementioned interventions entail frequent aversive oral/facial sensory inputs, such as suctioning of secretions and use of tape on the face to hold the feeding tube and/or endotracheal tube in place (Comrie & Helm, 1997; McGrath & Braescu, 2004; VandenBerg, 1990). As a consequence, the infants may adapt by exhibiting excessive aversion to any oral or facial stimulation (Comrie & Helm, 1997; Harris, 1986; VandenBerg, 1990).

Infants in the neonatal intensive care unit (NICU) encounter many negative external factors which are part of their physical surrounding that influence their behavioral responses to the feeding experience (McGrath & Braescu, 2004; Thoyre, 2003; VandenBerg, 1990). For instance, they are physically separated from their mothers,

they have multiple caregivers, and they are exposed to bright lights and loud noises from medical equipment (Als et al., 1996; Gardner & Hagedorn, 1991; VandenBerg, 1990). These factors have been identified as potential contributors to the disorganization, distress and irritability that preterm infants often manifest during oral feeding (Gardner & Hagedorn, 1991; Thoyre, 2003; VandenBerg, 1990).

2.5 Current clinical management of neonatal oral feeding

A large proportion of clinical practices in North America use the "Developmental Care Approach" as a conceptual framework for the clinical management of oral feeding in the NICU (Als, 1996; Mahoney & Cohen, 2005; Premji et al., 2004; Ross & Browne, 2002). Developmental care is an approach which employs a range of medical and nursing interventions aimed at promoting development and preventing morbidity in preterm infants (Symington & Pinelli, 2003). Examples of developmental care strategies include: assessing and observing infants' physiological and behavioral state to determine when to provide interventions; clustering of medical and nursing care activities to reduce interrupting infants during rest/sleep periods; providing supportive behavioral techniques e.g. NNS, music and kangaroo care (skin to skin) to encourage appropriate development; integrating parent involvement in their infant's care, e.g. allowing them to bathe and feed their infant, to empower parents; and control of environmental stressors, e.g. reducing lights and sounds, to diminish infant distress (Symington & Pinelli, 2003; Westrup, Stjernqvist, Kleberg, Hellstrom-Westas, & Lagercrantz, 2002).

In keeping with the Developmental Care Approach, management of oral feeding, i.e. determining readiness to start oral feeding and advancing oral feedings, is based on both nurses' and physicians' clinical observations and judgment (McGrath & Braescu,

2004; Premji et al., 2004; Shaker, 1999). More specifically, preterm infants receive their nutrients via tube feeding until they are deemed able to feed safely by mouth (McCain, 2003; McCain, Gartside, Greenberg, & Lott, 2001). Recent studies and two national surveys revealed there is no consensus on the criteria to commence oral feeding, and it is often based on clinical examination and judgment (Kinneer & Beachy, 1993; McGrath & Braescu, 2004; Siddell & Froman, 1994; White-Traut et al., 2005). Some nurseries will introduce oral feeding to preterm infants at around 33-34 weeks PMA when their sucking pattern begins to resemble that of full term infants (McGrath & Braescu, 2004; Siddell & Froman, 1994). However, others will use preterm infants' behavioral cues to assess readiness, such as wakefulness, NNS ability, and signs of hunger e.g. crying and thumb sucking (McCain, 2003; McGrath & Braescu, 2004; Shaker, 1999; White-Traut et al., 2005). Objective evidence on the accuracy of these criteria to reflect oral feeding readiness in preterm infants is lacking.

Once oral feeding is initiated, infants are gradually weaned from tube to independent oral feeding (Thoyre, Shaker, & Pridham, 2005). The criteria to advance oral feedings are also based on nurses' and physicians' observations of infants' oral feeding performance e.g. overall milk intake and feeding duration, and on their physiological and behavioral responses e.g. episodes of apnea, bradycardia, oxygen desaturation, choking, gagging, and vomiting during oral feeding (Premji et al., 2004; Shaker, 1999). Research evidence on the validity of these criteria for advancing oral feeding is very limited.

On average, preterm infants make this transition from complete tube to independent oral feeding within 6-19 days (Thoyre et al., 2005). However, several factors have been noted to prolong the progression to independent oral feeding in preterm

infants. These include oral feeding difficulties, immaturity (younger GA), number of neonatal morbidities, number of days on tube feeding, and duration of ventilator support (Bazyk, 1990; Hawdon et al., 2000; Pickler, Mauck, & Geldmaker, 1997; VandenBerg, 1990).

In terms of minimizing the risks for oral feeding difficulties, very little attention is paid to safeguarding oral feeding skills despite the fact that the Developmental Care Approach focuses on prevention of neonatal morbidity (Burklow et al., 2002; McGrath & Braescu, 2004; Premji et al., 2004). One exception is the non-standardized provision of NNS opportunities. Current practice for the management of oral feeding is to consult feeding specialists only when problems arise with the transition from tube to independent oral feeding (Bazyk, 1990; Harris, 1986; Morris, 1989; Premji et al., 2004). Feeding specialists evaluate the infant to identify the underlying problems and then develop individual treatment plans (Clark et al., 2003; Harris, 1986; Wolf & Glass, 1992). This current approach is inefficient because at the time when feeding specialists are consulted there is great pressure from the medical staff to discharge the infant from the hospital expecting that all feedings be taken by mouth (Burklow et al., 2002; Harris, 1986; Hunter, 2001). Such demands entail that infants must be rapidly transitioned to independent oral feeding. However, the treatment of oral feeding difficulties is a slow process requiring frequent and prolonged interventions (Harris, 1986; Morris, 1989; Vogel, 1986). Feeding specialists are recognizing the need to change the current practice, and to start intervening before oral feeding problems are clinically established, in order to safeguard and promote appropriate development of oral-motor skills (Bazyk, 1990;

Burklow et al., 2002; Calvert et al., 1985; Gorga, 1994; Hawdon et al., 2000; Ross & Browne, 2002).

As stated before, the concept of developmental care emphasizes promoting development and preventing morbidity in preterm infants (Symington & Pinelli, 2003). However, the present clinical management of oral feeding is centered on a therapeutic approach rather than a preventative approach (Burklow et al., 2002; McGrath & Braescu, 2004). A preventative approach can optimize neonatal oral feeding skills and reduce/prevent neonatal oral feeding problems (Fucile et al., 2002, 2005). Further investigations on the efficiency of early intervention strategies in the NICU aimed at optimizing oral feeding skills in preterm infants are critically needed.

2.6 Early Intervention-Sensorimotor stimulation

Very preterm infants (less than 32 weeks GA) may spend anywhere from 19 to over 100 days in the NICU to achieve physiological stability, adequate growth, and appropriate neurodevelopment (Gilbert, Nesbitt, & Danielsen, 2003; St. John et al., 2000). Therefore, the NICU becomes an important environment for early intervention (Gorski, 1991; Liaw, 2000). Early intervention in the literature is defined as provision of services to optimize infants' development and promote positive parenting (Anderson, 1986; Blauw-Hospers & Hadders-Algra, 2005; Gorski, 1991; Ramey, Bryant, & Suarez, 1990). Sensorimotor stimulation is one type of early intervention that may be used to optimize preterm infants' development. It consists of providing developmentally appropriate sensory inputs, including oral, tactile, kinesthetic, vestibular, auditory, olfactory, and visual, in order to maintain and/or facilitate infants' development (Dieter & Emory, 1997; Korner, 1990). It is also referred to in the literature as sensory stimulation,

sensory intervention, supplemental stimulation, and modification of external stimuli (Anderson, 1986; Field, 1988; Hunter, 2001; Symington & Pinelli, 2003).

2.6.1 Historical overview of practice approach

Changing theories about the suitability of sensorimotor stimulation in preterm infants have strongly influenced clinical practice and research advancement in this area (Hunter, 2001). In the 1940s and 1950s, preterm infants were considered too fragile to tolerate any stimulation, and thus minimal stimulation was prescribed for them (Hunter, 2001; Korner, 1990).

In the 1960s and early 1970s, the scarcity of stimuli in these early nurseries precipitated the sensory deprivation theory, whereby behavioral scientists believed that infants in the NICU were deprived of beneficial sensory stimuli (Hunter, 2001; Scarr-Salapatek & Williams, 1973). In turn, this led to the institution of supplemental stimulation programs in clinical practice and extensive research in this area (Field, 1980; Hunter, 2001; Scarr-Salapatek & Williams, 1973).

However, in the later 1970s and early 1980s behavioral scientists learned that instead of being sensory deprived, preterm infants were bombarded by diverse sensory stimuli in the NICU, such as bright lights, noisy medical equipment, frequent handling for medical procedures, and multiple caregivers (Cornell & Gottfried, 1976; Hunter, 2001; Leib, Benfield, & Guidubaldi, 1980). A sensory overload theory emerged which hypothesized that the nursery environment overwhelms infants with its multiple sensory stimuli (Cornell & Gottfried, 1976; Hunter, 2001; Leib et al., 1980). Consequently, there was a decline in the provision of supplemental stimulation in NICUs and a decrease in research in this area (Hunter, 2001).

In the late 1980s and 1990s, emerging concerns about the large quantity and variety of random stimuli prompted the rise of “environmental neonatology” in which the influence of animate and inanimate factors in NICUs were being explored (Als, 1986; Hunter, 2001; Linn, Horowitz, & Fox, 1985). Studies found that the types, intensity and amount of nursery stimuli were unsuitable and/or inappropriate for developing preterm infants (Gottfried et al., 1981; Linn et al., 1985; White-Traut, Nelson, Burns, & Cunningham, 1994). Consequently, the “Developmental Care Approach” has emerged which emphasizes the provision of only necessary interventions that will promote development, while protecting the infant from unnecessary stress and disturbances, as previously discussed (Als, 1986; Gorski, 1991; Mahoney & Cohen, 2005).

At present, there is resurgence among health care professionals that recognizes the value of developmentally appropriate sensorimotor stimulation. A current national survey in the United States reported that 38-96% of NICUs surveyed provide some form of sensorimotor stimulation intervention, such as massage, music, gentle rocking, waterbeds, and NNS on a pacifier (Field, Hernandez-Reif, Feijo, & Freedman, 2006). Although, there is an increased application of sensorimotor stimulation in NICUs, empirical evidence for its effectiveness in younger and more medically fragile preterm infants is lacking.

2.6.2 Theoretical framework

The theoretical framework of sensorimotor stimulation stems from the neurodevelopment-environment interaction perspective (Als, 1996). According to this perspective, brain development is primarily influenced by genetics. However, environmental inputs may also influence brain development (i.e. neuronal organization

and connections as well as neurochemical growth and sensitivities) through infants' various senses, such as tactile, kinesthetic, vestibular, visual, auditory, olfactory and gustatory (Als, 1986, 1989, 1996; Kandel, Schwartz, & Jessel, 2000; Sizun & Westrup, 2004; Spinelli, 1987).

Accordingly, provision of sensorimotor stimulation in preterm infants is based on the notion that the maternal womb is the ideal environment for optimizing infants' development (Als, 1989; 1996). In utero infants are exposed to continuous cutaneous-tactile input from the amniotic fluid, motoric-kinesthetic input within the amniotic sac wall, and maternal diurnal rhythms. As well, they are in a protective environment that attenuates sensory inputs to the developing sense organs (Als, 1989; 1996). It is postulated that this in utero environment provides all the necessary sensory stimulation for maximizing infants' developmental outcome (Als, 1989, 1996). Preterm birth not only disrupts the normal developmental trajectory, but it places infants in a highly technological environment. Although this technological environment is necessary for their survival, it exposes them to developmentally unsuitable stimuli, such as invasive medical procedures (e.g. suctioning of secretions, heel stick for blood drawing), bright lights, loud noises, decreased positive tactile touch, prolonged separation from their mother, and multiple caregivers (Als, 1986, 1996; Korner, 1990). Exposure to such factors at a time of rapid brain development may alter neuronal organization and neurochemical growth. This in turn, may negatively influence later development (Als, 1986, 1996; Korner, 1990). Therefore, provision of positive sensorimotor stimulation may promote proper neuronal organization and/or neurochemical growth leading to proper developmental outcomes (Als, 1996; Korner, 1990).

Importantly, the sensorimotor stimulation provided must be developmentally appropriate i.e. meet the needs of infants and not cause undue stress to them (Gorski, 1991; Hadders-Algra, 2000; Korner, 1990; Mahoney & Cohen, 2005). The human sensory system matures and becomes functional in an orderly sequence (Gottlieb, 1976). Tactile/cutaneous sensory function is first achieved in the oral region and whole body at 8 to 32 weeks of gestation, respectively (Gottlieb, 1976). The vestibular system develops at 8 weeks gestation, followed by the auditory system which develops at 16-24 weeks gestation, and finally the visual systems develops at 31-32 weeks gestation (Gottlieb, 1976). The literature indicates that the two senses that are least developed in preterm infants i.e. the auditory and visual systems, are overly stimulated in the nursery (White-Traut et al., 1994). However, the more developed senses i.e. tactile/cutaneous and vestibular systems are infrequently and/or inappropriately stimulated in the nursery (White-Traut et al., 1994). Taking the above into consideration, provision of tactile/cutaneous sensorimotor input to the oral structures and whole body appears to be suitable for optimizing developmental outcomes, particularly oral feeding skills.

The beneficial effects of early tactile/cutaneous sensorimotor stimulation in the rat model are well established. Kuhn & Schanberg (1998) and Schanberg & Field (1987) have demonstrated that physical contact with the young in the immediate postnatal period is essential for normal growth and development in the rat pup. Disruption of the mother-infant physical bond causes marked physiological and behavioral changes. These include reduction in tissue ornithine decarboxylase (a sensitive index of cell growth and differentiation implicated in the synthesis of DNA), fall in growth hormone release in all body organs, loss of tissue sensitivity to growth hormone, growth retardation and

developmental delay. These investigators found that simulating the tongue-licking behavior of the mother, by stroking the pup with a foam paint brush, reversed all of the above adverse effects. These findings suggest that early tactile/cutaneous sensorimotor stimulation can elicit neuro-physiological responses which are essential for proper growth and development of the rat pup (Kuhn & Schanberg, 1998; Schanberg & Field, 1987).

A parallel may be drawn with the human model, as preterm infants in the NICU are physically separated from their mother for a prolonged period of time and often have medical interventions/equipment such as tube feedings, endotracheal tubes, and umbilical intravenous lines which interfere with mother-infant bonding (Scarr-Salapatek & Williams, 1973; Schanberg & Field, 1987). As a result, they are deprived of the continuous positive and nurturing contact that healthy infants are regularly exposed to (Scarr-Salapatek & Williams, 1973; Schanberg & Field, 1987). Although studies on human infants are less definitive, oral feeding difficulties, growth failure, failure to thrive, developmental delay, and delayed attachment to the parent are common problems in the preterm population (Gardner & Hagedorn, 1991; Hack & Fanaroff, 1999; Mainous, 2002). Inadequate and inappropriate stimulation have been implicated as contributors to these problems, as discussed above (Als, 1996; Korner, 1990; Mainous, 2002). Hence, provision of developmentally appropriate sensorimotor stimulation, specifically of a tactile/cutaneous nature can influence neuronal development, in turn optimizing the development of oral feeding skills in this high risk group (Als, 1996; Bond, 2002; Korner, 1990; Mainous, 2002).

2.7 Oral stimulation

Oral stimulation is the most commonly utilized and researched sensorimotor intervention to improve preterm infants' oral feeding skills. Oral stimulation may consist of oral support, NNS, and/or oral sensorimotor input (Anderson, 1986; Einarsson-Backes, Deitz, Price, Glass, & Hays, 1994; Harris, 1986). The overall goals of oral stimulation are to maintain rudimentary oral-motor skills, enhance oral muscle tone and movement, and facilitate normal oral-motor developmental patterns (Anderson, 1986; Bond, 2002; Korner, 1990).

2.7.1 Oral support

Oral support aims to ameliorate the NS pattern by providing stability to buccal pads and the jaw (Einarsson-Backes et al., 1994; Hill, 2005; Hill, Kurkowski, & Garcia, 2000). Bobath (1980) theorized that stability must be developed before mobility. Based on this notion, it is suggested that when the mandible is stable, the tongue is then able to move with greater control (Einarsson-Backes et al., 1994; Hill, 2005; Hill et al., 2000). This is achieved by placing the middle finger under the chin, and the thumb and index fingers on the cheek. Einarsson-Backes et al. (1994) demonstrated an increase in the volume of milk taken when oral support was provided during the first two minutes of nipple feeding in 13 preterm infants (range 34-40 weeks GA). Hill et al. (2005; 2000), using a Whitney Mercury Strain Gauge, reported an improved sucking pattern as evidenced by shorter and less frequent sucking pauses when oral support was provided during the first and final 3 minutes of nipple feeding in 20 preterm infants (mean 30 weeks GA). While oral support appears to have beneficial effects on preterm infants' oral feeding performance, the small sample sizes and older gestational ages of participants do not

permit generalization of results to younger ages (Einarsson-Backes et al., 1994; Hill, 2005; Hill et al., 2000). Moreover, the short data collection period (2 and 6 minutes) prevents examination of oral support over an entire feeding session (Einarsson-Backes et al., 1994; Hill, 2005; Hill et al., 2000). Studies over an entire oral feeding session, with a larger and younger sample, are needed to establish the effect of oral support.

2.7.2 Non-nutritive sucking

NNS is primarily used to facilitate the development of sucking activity, improve behavioral state, and enhance digestion of enteral feeds (Hill, 2005; Pinelli & Symington, 2005). NNS opportunities can be provided during tube feeding and before tube/oral feeding (Pinelli & Symington, 2005). These two NNS opportunities are very different. When NNS is provided during tube feeding infants may learn the association between sucking and feeding satiation, and when it is provided before tube/oral feeding it may prepare the infant for nipple feeding and help promote appropriate behavioral states for oral feeding (McCain, 1995; Pickler, Higgins, & Crummette, 1993; Pickler & Reyna, 2004).

Several studies have shown that NNS during tube feeding promotes earlier readiness for bottle feeding, accelerates the transition from tube to independent oral feeding, leads to greater suction amplitudes and number of sucks per burst, and decreases length of hospital stay (Bernbaum, Pereira, Watkins, & Peckham, 1983; Field et al., 1982; Measel & Anderson, 1979; Sehgal, Prakash, Gupta, Mohan, & Anand, 1990). Inconsistent outcomes were found for the effect of NNS during tube feedings on weight gain, gastrointestinal motility and stool frequency (Bernbaum et al., 1983; Ernst et al., 1989; Sehgal et al., 1990). These inconsistencies appear to be related to the different

methodologies used across studies. Bernbaum et al., (1983) and Sehgal et al., (1990) both provided NNS from the start of tube feeding up until infants achieved independent oral feeding. Ernst et al., (1989) provided NNS only until infants commenced oral feeding.

When NNS was provided before tube/oral feeding several studies found that it resulted in an increased percentage of prescribed milk taken, and it promoted a more organized behavioral state, such as increased quiet awake states, decreased restlessness and fussiness in preterm infants (Gill, Behnke, Conlon, McNeely, & Anderson, 1988; McCain, 1995; Pickler, Frankel, Walsh, & Thompson, 1996; Pickler & Reyna, 2004).

These studies highlight the multitude of beneficial effects of NNS on preterm infants' oral feeding performance. However, the majority of the studies were carried out in the 1980s and 1990s when preterm infants were older and less medically fragile than the current population of survivors. The favorable outcomes associated with NNS makes it important to research its effect on the increasing number of younger preterm born infants.

2.7.3 Oral sensorimotor input

Oral sensorimotor input is mainly used to improve sucking skill, to enhance oral muscle strength and movement, and to maintain normal oral sensory responses (Anderson, 1986; Harris, 1986). Oral sensorimotor input is described as stroking to the peri- and intra-oral structures, such as the cheeks, lips, jaw, tongue, palate and gums (Harris, 1986). Beneficial effects of oral sensorimotor input have been reported by several studies. Leonard and colleagues (1980) investigated the impact of stroking the cheeks for 4 minutes during the oral feeding session of 5 neonates 27-40 weeks GA. They found an increase in sucking rate, defined as number of sucks/minute, when the oral

sensorimotor input was provided. Gaebler & Hanzlik (1996) investigated the effects of oral sensorimotor input, consisting of stroking the cheeks, lips, and gums for 2 minutes, 3 times per day until independent oral feeding was attained. Preterm infants (30-34 weeks GA) receiving this treatment required fewer tube feedings, scored better on the revised Neonatal Oral Motor Assessment Scale, had greater weight gain, and had fewer days of hospitalization. Although these studies demonstrated that oral sensorimotor input can enhance preterm infants' oral feeding performance, several limitations have been identified. The instrumentation used i.e. the revised Neonatal Oral Motor Assessment Scale was not tested for reliability and validity (Gaebler & Hanzlik, 1996), there was no blinding of the intervention (Gaebler & Hanzlik, 1996) and the sample sizes were small (Gaebler & Hanzlik, 1996; Leonard et al., 1980). Furthermore, both interventions were provided concomitant with oral feeding, and thus oral feeding difficulties may have already been established.

In an earlier study, we examined the effect of a pre-feeding oral stimulation, administered prior to the start of oral feeding, on preterm infants born less than 30 weeks gestation (Fucile, Gisel, & Lau, 2002). We demonstrated that 15 minutes of oral stimulation, which consisted of oral sensorimotor input and NNS, once a day, for 10 days, accelerated the transition from tube to independent oral feeding, increased overall milk intake, and enhanced rate of milk transfer. These findings were attributed to advanced sucking skills, in particular amplitude of the expression component of sucking (Fucile, Gisel, & Lau, 2005). In support of this, Rocha et al., (2006) who administered a similar oral stimulation protocol demonstrated that preterm infants 26-32 weeks GA started oral feeding earlier, reached independent oral feeding earlier, and were discharged

from the hospital earlier than controls. These studies clearly illustrate the benefits of pre-feeding oral stimulation on preterm infants' oral feeding performance. However, with the extensive social and economic consequences related to neonatal oral feeding difficulties, it remains imperative to continue the search for more efficacious early sensorimotor interventions.

2.8 Tactile/kinesthetic stimulation

Oral feeding, as depicted in the model (Appendix 2B), is a highly integrated multifaceted process (Burklow et al., 2002; McGrath & Braescu, 2004). Although, oral stimulation is the most common sensorimotor input administered to enhance preterm infants' oral feeding skills, it aims solely to improve the functioning of oral structures, i.e. sucking. Given the complexity of oral feeding, it has been postulated that other forms of sensorimotor input, such as tactile (touch to body), kinesthetic, auditory, olfactory and visual stimulation may also enhance preterm infants' oral feeding performance (Dieter & Emory, 1997). Specifically, these alternate forms of sensorimotor stimulation facilitate the development of associated systems, beyond the oral structures, and so may enhance the oral feeding process (Dieter & Emory, 1997; Korner, 1990).

There is evidence that tactile/kinesthetic stimulation, which consists of stroking the head, neck, limbs and trunk, along with passive range of motion to all the limbs enhances other associated systems related to oral feeding (Field et al., 1986). Several studies have found that preterm infants who received 15 minutes of tactile/kinesthetic stimulation 3 times per day, for 10 days, had better motor activity, weight gain, gastrointestinal motility, more alert behavioral states, and better neurobehavioral organization than those who did not receive the intervention (Diego, Field, & Hernandez-

Reif, 2005; Field et al., 1986; Mathai, Fernandez, Mondkar, & Kanbur, 2001; Scafidi, Field, & Schanberg, 1993). Enhancement of motor activity, gastric motility, and behavior state elicited by tactile/kinesthetic stimulation may also contribute to the oral feeding process, as illustrated in the model (Appendix 2B). Indeed, Rausch (1981) demonstrated that preterm infants who received 15 minutes of tactile/kinesthetic stimulation, once a day, for 10 days took a significantly greater volume of milk per day and had increased stool frequency compared to control infants. White and Labarba (1976) also found an increase in volume of milk ingested per day, decreased frequency of oral feeding per day, and an increase in average daily weight gain in infants who received 15 minutes of tactile/kinesthetic stimulation, 4 times per day, for 10 days. The above two studies suggest that tactile/kinesthetic stimulation may be an effective non-oral sensorimotor intervention contributing to oral feeding skills of preterm infants. However, these results are limited because the author did not delineate whether volume intake was via tube or oral feeding method (Rausch, 1981), there was no randomization (White & Labarba, 1976), and there was no blinding of intervention (White & Labarba, 1976). Further studies are needed to clearly establish the effect of tactile/kinesthetic stimulation on preterm infants' oral feeding skills.

2.9 Multi-sensorimotor stimulation

Uni-sensorimotor stimulation (i.e. one type of stimulation) may have beneficial effects beyond its targeted area, and therefore, may have favorable outcomes on multiple systems (Dieter & Emory, 1997; Korner, 1990). Accordingly, different types of uni-sensorimotor stimulations may have common beneficial outcomes. For instance, Bernbaum et al. (1983) demonstrated that NNS during oral feeding not only improved

sucking skills, but also enhanced gastrointestinal motility and weight gain. Field et al., (1987; 1986) demonstrated that tactile/kinesthetic stimulation improved weight gain, behavioral state organization, and motor development. Thus, it is conceivable that the simultaneous provision of multi-sensorimotor stimulations (i.e. more than 1 type of stimulation), such as oral plus tactile/kinesthetic may have an additive or synergistic effect leading to better oral feeding skills than that of uni-sensorimotor stimulation.

The notion that multi-sensorimotor stimulations, may further impact the oral feeding skills of preterm infants is partially supported. White-Traut and colleagues (2002) demonstrated that preterm infants, who received 15 minutes of auditory, tactile, vestibular and visual stimulation twice a day, from 33 weeks PMA until hospital discharge, had greater volume intake, transitioned 4 days sooner from tube to independent oral feeding, and were discharged from the hospital earlier than control infants. The improvements in oral feeding and in the earlier hospital discharge were attributed in part to enhanced alertness during the oral feeding session. However this was a retrospective study, so results may be biased by confounding variables that were not controlled for. Moreover, the authors did not distinguish between the individual effects of the multi-sensorimotor stimulations. In another study, White-Taut et al., (1997) investigated the impact of two uni- stimulations (auditory or tactile) and two multi-stimulations (auditory, tactile, and visual; auditory, tactile, visual and vestibular) on infants' physiological response, including pulse rate, respiratory rate, oxygen saturation, and behavioral state to get a better understanding on the safety of uni- and multi-stimulation. The authors found that infants' physiological responses remained within normal limits in all study groups, suggesting that uni- and multi- stimulations are safe and

not compromising the infant. However, specific clinical outcomes such as oral feeding performance, motor function, and weight gain following the stimulation were not assessed. In spite of these study limitations, results from these two studies provide evidence for favorable effect(s) of multi-sensorimotor stimulations on preterm infants' oral feeding skills. A prospective study where uni- versus multi-sensorimotor stimulations are compared, would establish more conclusively whether multi forms of sensorimotor stimulation have an additive or synergistic effect on the oral feeding skills of preterm infants.

2.10 Summary of literature review

- Preterm infants are at high risk of encountering oral feeding difficulties. Neonatal oral feeding difficulties remain a prominent issue because of their potential impact on length of hospitalization, parent-infant bonding and long-term oral feeding disorders.
- Current clinical management of oral feeding focuses on a rehabilitative approach i.e. remediation of problems once they are clinically established. This approach is inefficient. A preventative approach, whereby early intervention strategies aim to facilitate the appropriate development of oral feeding skills, is critically needed.
- Sensorimotor stimulation is one type of early intervention which can be used to optimize the development of preterm infants' oral feeding skills. Oral feeding is a highly complex integrated multiple systems process. Hence, many forms of sensorimotor intervention may be used to enhance preterm infants' oral feeding performance.

- Oral stimulation is the most common sensorimotor stimulation used. Oral stimulation, administered prior to the start of nipple feeding, enhances the oral feeding skills of preterm infants. However, more efficacious early sensorimotor stimulations are needed to further prevent/reduce oral feeding difficulties, and thus, decrease the burden of care.
- Tactile/kinesthetic stimulation aimed at improving preterm infants' growth and motor development may also enhance oral feeding skills. Further studies are needed to clearly establish the effect of tactile/kinesthetic stimulation on preterm infants' oral feeding skills.
- Provision of multi-sensorimotor stimulations such as, oral plus tactile/kinesthetic, may have an additive or synergistic effect on infants' oral feeding skills, which may lead to better oral feeding skills compared to either uni-sensorimotor stimulation, such as oral or tactile/kinesthetic alone.

2.11 References

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CHAPTER 3

RATIONALE, OBJECTIVES, AND STUDY DESIGN

3.1 Rationale

Oral feeding is an innate skill for healthy full term newborns (Lemons & Lemons, 1996; Miller & Kiatchoosakun, 2004). However, for infants who are born prematurely, oral feeding is a gradual developmental process dependent on their neurological maturity and their physical and social surroundings (Lemons & Lemons, 1996; Miller & Kiatchoosakun, 2004). Preterm infants face several challenges for successful oral feeding, such as immature/disorganized sucking skills, inability to coordinate sucking, swallowing and respiration, decreased alert behavioral state, and poor endurance (Comrie & Helm, 1997). Neonatal oral feeding difficulties impede the transition to oral feeding, prolong hospitalization, and increase parental stress (Bazyk, 1990; Burklow et al., 2002; Schanler et al., 1999). Financial constraints and the push towards earlier hospital discharge underscore the urgent need to change the current focus of care from a rehabilitative approach to a more preventative approach so as to minimize these negative consequences. Development of novel and efficient early intervention strategies focusing on safeguarding and optimizing oral feeding skills of preterm infants are critically needed.

Sensorimotor stimulation is one form of intervention that may be used to facilitate the acquisition of appropriate oral feeding skills during infants' hospital stay in the neonatal intensive care unit (NICU). Oral stimulation, aimed at improving the function of oral-motor function only, is the most common sensorimotor stimulation in current use. It

is usually initiated after feeding problems have become established. There is evidence that pre-feeding oral stimulation, before the start of oral feeding, is an effective early intervention to facilitate the development of oral feeding skills (Fucile et al., 2002; Rocha et al., 2006). However, the complexity of neonatal oral feeding difficulties necessitates more efficacious early sensorimotor interventions to further reduce/prevent neonatal oral feeding difficulties in this highly vulnerable population.

Oral feeding is a multiple system process involving the maturation, function, and interaction of the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral and neurological systems. Consequently, oral feeding is not only influenced by the oral-motor system, but by any of these associated systems. It is proposed that alternate forms of sensorimotor interventions, in particular tactile/kinesthetic stimulation, may facilitate the development of associated systems and thereby advance oral feeding skills. However, there is a paucity of evidence demonstrating that tactile/kinesthetic stimulation enhances oral feeding skills. As such, the effect of pre-feeding tactile/kinesthetic stimulations, prior to the start of nipple feeding, needs to be further investigated.

Insofar as different forms of sensorimotor stimulations may have common benefits (Dieter & Emory, 1997), it is conceivable that simultaneous provision of multi-sensorimotor input such as, oral plus tactile/kinesthetic may have an additive or synergistic effect on infants' oral feeding skills. This should lead to improved oral feeding performances compared to uni-sensorimotor stimulation i.e. oral or tactile/kinesthetic singly. There is limited evidence to support this notion. Therefore, assessing and comparing the effect of uni- versus multi-sensorimotor intervention will be important, in order to provide more efficacious preventative oral feeding interventions.

3.2 Objectives

The objectives of this study were:

1. To assess the effect of a pre-feeding uni-oral (O), uni-tactile/kinesthetic (T/K), and multi-oral plus tactile/kinesthetic (O+T/K) stimulation, administered prior to the start of nipple feeding, on the oral feeding skills of preterm infants.
2. To compare the impact of a pre-feeding multi-O+T/K stimulation to a uni-O or uni-T/K stimulation on the oral feeding skills of preterm infants.

3.3 Hypotheses

The following hypotheses were tested:

1. Preterm infants who receive a pre-feeding uni-O, uni-T/K, or multi-O+T/K stimulation, before the introduction of nipple feeding, will demonstrate more advanced oral feeding skills than those who did not receive any intervention.
More specifically, they will demonstrate:
 - 1a. enhanced oral feeding performance.
 - 1b. more mature nutritive sucking skills.
 - 1c. better coordinated suck-swallow-respiration processes.
 - 1d. enhanced growth and motor function.
2. Preterm infants who receive a pre-feeding multi-O+T/K stimulation will display better oral feeding skills over those who receive uni-O or uni-T/K stimulation.

3.4 Specific aims

In line with the hypotheses, the aims of this study were:

- 1a. To assess the effect of a pre-feeding uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' oral feeding performance, including time to attainment of independent oral feeding (primary outcome), proficiency, volume transfer, rate of transfer, and volume loss.
- 1b. To explore the effect of a pre-feeding uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' nutritive sucking skills, in particular: stage of sucking pattern, sucking burst duration, sucking rate, and suction and expression amplitudes.
- 1c. To determine the effect of a pre-feeding uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' suck-swallow-respiration coordination, including ratio of number of sucks to swallows, stability of suck-swallow interval, and swallow-respiration pattern.
- 1d. To explore the effect of a pre-feeding uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' growth (weight gain), motor function (postural alignment, head and trunk control, and limb movements) and length of hospital stay.
2. To determine whether a pre-feeding multi-O+T/K stimulation leads to better oral feeding performance, nutritive sucking skills, suck-swallow-respiration coordination, growth, motor function, and shorter length of hospitalization than a uni-O or uni-T/K stimulation alone.

3.5 Research design overview

A prospective randomized clinical trial was performed to assess and compare the effect of a pre-feeding uni-O, uni-T/K, and multi-O+T/K intervention on preterm infants' oral feeding skills. The target population consisted of clinically stable preterm infants. Infants meeting the following criteria were enrolled: born between 26-32 weeks gestational age (GA); appropriate size for their GA; on all tube feedings; with no chronic medical complications, including severe bronchopulmonary dysplasia, intraventricular hemorrhages grades III or IV, periventricular leukomalacia, or necrotizing enterocolitis; and with no congenital anomalies (e.g. oral and cardiac). Infants with chronic medical complications and congenital anomalies were excluded because it is important to establish 'proof of principle' first before applying this preventative approach to more vulnerable infants.

The participants were recruited from the NICU at Texas Children's Hospital, Houston, TX. The hospital is a tertiary care center. The nurseries at Texas Children's Hospital include a level III care unit consisting of 70 beds, and a level II care unit consisting of 80 beds. The Institutional Review Board for Human Subject Research of Baylor College of Medicine and Affiliated Hospitals approved the research protocol (Appendix 3A).

Informed parental consent to participate was given by parents, prior to participants' entry into the study (Appendix 3B). Randomization was carried out using a sealed envelope system. Infants were randomized, after discontinuation of nasal continuous positive airway pressure, into either one of the following study groups: uni-O, uni-T/K, multi-O+T/K, and control. Stratification by GA (26-29 and 30-32 weeks

gestational) was used to ensure that each group had similar age distribution. As well, stratification by time (per 3 months) was carried out to make certain each group had equal distribution of attending neonatologists.

The study investigated 3 sensorimotor stimulations and 1 control intervention: 1) uni-oral stimulation (Appendix 3C) – consisting of stroking the cheeks, lips, gums, and tongue and non-nutritive sucking on a pacifier, for 15 minutes, twice a day, using our previous protocol (Fucile et al., 2002). This particular uni-O stimulation was selected because in a previous studies we found it accelerated the transition from tube to oral feeding, enhanced overall milk intake and rate of milk transfer in preterm infants (Fucile et al., 2002); 2) uni-tactile/kinesthetic stimulation (Appendix 3D) – involving stroking the head, neck, trunk and limbs along with passive range of motion of the limbs, for 15 minutes, twice a day, based on the protocol by Field and colleagues (1986). This particular uni-T/K stimulation was selected because its procedures are well defined and safe. In addition, evidence of its beneficial effects on behavior state, motor development, and weight gain are well documented (Dieter, Field, Hernandez-Reif, Emory, & Redzepi, 2003; Field et al., 1987; Field et al., 1986); 3) multi-oral plus tactile/kinesthetic stimulation (Appendix 3E) – consisting of the same oral and tactile/kinesthetic stimulation, described above, for 15 minutes, each once per day in random order, and 4) control intervention (Appendix 3F) – involving the researcher (the candidate, SF) placing her hands in the isolette but not touching the infant, for 15 minutes, twice a day. This particular control intervention was designed to eliminate any possible effects of the daily presence of the researcher at the bedside. No human touch during the intervention was provided to this group because static touch i.e. placing of hands on infants' head and

abdomen has been shown to have physiological benefits, specifically a decrease in oxygen requirement, and also to promote a more organized behavioral state in preterm infants 27-32 weeks GA (Jay, 1982). Such benefits might in turn enhance preterm infants' oral feeding skills.

The researcher provided all interventions while infants remained in the isolette. All interventions were commenced 48 hours post nasal continuous airway pressure and administered for 10 days, within a 14 day period. Interventions were not provided or halted if infants presented signs of medical instability. Data on infants' responses during the intervention were collected. A screen was placed around the infants' isolette to blind caretakers and family members to group assignment.

Infants' oral feeding skills were monitored (Appendix 3G), including: 1) oral feeding performance - time to attainment of independent oral feeding (days, primary outcome), proficiency (%), volume transfer (%), rate of transfer (ml/min), and volume loss (ml); 2) nutritive sucking skills - stage of sucking pattern, sucking burst duration (sec), sucking rate (number suction and/or expression per sec), and suction and expression amplitudes (mmHg); 3) suck-swallow-respiration coordination - ratio of number of sucks to swallows, stability of suck-swallow interval (sec), and occurrence of swallow-respiration pattern (%); 4) growth-mean daily weight gain in g/kg/day; 5) motor function - postural alignment, head and trunk control, and limb movement were assessed using the Test of Infant Motor Performance (Campbell, 2001); and 6) length of stay at the hospital (days). Oral feeding performance, nutritive sucking skills, and suck-swallow-respiration coordination outcomes were monitored at three oral feeding sessions, when infants were taking 1-2, 3-5, and 6-8 oral feedings per day. A nipple bottle apparatus was

used to monitor sucking, swallowing and respiration during oral feeds (Appendix 3H). Mean daily weight gain was monitored before, during, and after the sensorimotor interventions, and motor function was monitored at the end of the sensorimotor interventions, i.e. prior to the start of oral feeding.

To ensure results were not biased the following variables were monitored: severity of illness, number of infants who received all and/or partial breast-feeding and co-interventions (occupational, physical and speech therapy), and number of parental visits. As well, postmenstrual age, weight, behavioral state, and occurrence of apnea, bradycardia, and oxygen desaturation during the monitored oral feedings were noted. To make certain results were not influenced by a possible Hawthorne effect, such as the additional daily presence of a research person at the bedside, data on the primary outcome were gathered by chart review for 10 additional infants who received standard nursery care, named 'Hawthorne group'.

All infants were monitored from the start of the study (i.e. the commencement of the sensorimotor interventions) until hospital discharge. The attending neonatologist was responsible for initiating and advancing oral feeding. Nurses were responsible for feeding and weighing the infants in their customary manner. Both professionals were blind to group assignment.

Sample size was calculated based on a type 1 error of 0.05 and a power of 0.80. Sample size estimation was derived from the primary outcome, time to attainment of independent oral feeding, which at Texas Children's Hospital averaged 14 ± 8 days (Fucile et al., 2002). A decrease of 8 days (1 SD) to attain independent oral feeding was considered a clinically important effect. Thus, a sample size of 64 (16 participants per

group) was needed. However, an additional 30% of infants were enrolled to allow for infants who may develop serious medical illnesses, and would be too fragile to complete the study. These would be infants who had their tube or oral feedings stopped for greater than 7 consecutive days, developed severe bronchopulmonary dysplasia, intraventricular hemorrhages grades III or IV, periventricular leukomalacia, or necrotizing enterocolitis; after the start of the study. Therefore, 84 participants (21 infants per group) were recruited.

Continuous variables were analyzed using one-way ANOVA and repeated measures ANOVA. In cases of statistical significance post-hoc Bonferroni tests were used to assess differences between groups and time. Discrete variables were analyzed using Fisher's exact test. Significance was defined at the 0.05 level. Analyses were performed using the Statistical Program for Social Sciences software version 15.0 (SPSS, Inc., Chicago, IL).

3.6 References

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CHAPTER 4

INTRODUCTION TO MANUSCRIPT 1

“PRE-FEEDING SENSORIMOTOR INTERVENTIONS DECREASE THE TRANSITION TIME TO INDEPENDENT ORAL FEEDING IN PRETERM INFANTS”

Preterm infants are not only at risk for encountering oral feeding difficulties because of their immaturity, but also as a result of invasive medical interventions e.g. suctioning of secretions, and/or prolonged exposure to noxious environmental stimuli, such as bright lights and loud noises (Als, 1986, 1996; Becker, Grunwald, Moorman, & Stuhr, 1991). Exposure to such noxious stimuli at a time of rapid brain development may alter the neural differentiation of the brain which in turn may negatively influence infants' development (Als, 1986, 1996). An increased vulnerability to difficulties with breast/bottle feeding in preterm infants underscores the urgent need to develop early intervention strategies that will facilitate the appropriate development of their oral feeding skills and will prevent or reduce long-term oral feeding disorders (Burklow et al., 2002; Dodrill et al., 2004). Developmentally appropriate sensorimotor stimulation was selected as an early intervention strategy to counterbalance the potentially negative impact of prematurity and to enhance preterm infants' oral feeding skills (Korner, 1990).

Oral feeding is a multifaceted process involving the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral, and neurological systems. Sensorimotor stimulation aimed at enhancing one or more of these systems may in turn improve preterm infants' oral feeding performance (Dieter & Emory, 1997; McGrath & Braescu, 2004). Oral stimulation, the most commonly practiced and researched sensorimotor

stimulation has been found to ameliorate preterm infants' oral feeding performance (Fucile et al., 2002; Rocha et al., 2006). However, oral stimulation focuses only on improving oral-motor function. It remains unclear whether non-oral sensorimotor stimulations, specifically of a tactile/kinesthetic nature, which enhances other associated systems, such as motor activity, behavioral states and gastrointestinal function may also improve oral feeding performance (Dieter et al., 2003; Field et al., 1987; Mathai et al., 2001). It is conceivable that provision of multi-sensorimotor stimulation, in particular oral plus tactile/kinesthetic, may have additive or synergistic beneficial effects leading to better oral feeding performance than uni- sensorimotor stimulations. However, the effects of uni- versus multi-sensorimotor stimulations on oral feeding performance have not yet been examined.

This first manuscript, therefore, assesses the impact of a pre-feeding uni-oral, uni-tactile/kinesthetic, and multi-oral plus tactile/kinesthetic stimulation, administered prior to the start of oral feeding, on the oral feeding performance of preterm infants. A randomized clinical trial was conducted. All infants were randomized into a uni-oral, uni-tactile/kinesthetic, multi-oral + tactile/kinesthetic, or control group. To ensure results were not confounded by a possible Hawthorne effect, the oral feeding progression of another group of infants who only received standard care was monitored using a chart review. All infants were followed from the start of the study to hospital discharge. We prospectively examined the impact of each intervention on infants' oral feeding performance, specifically time to attainment of independent oral feeding, proficiency, volume transfer, rate of transfer, and volume loss. A better understanding of the impact of pre-feeding sensorimotor stimulations in this high risk population is essential so that

more cost-effective oral feeding interventions may be implemented to minimize oral feeding difficulties, and thereby improve the quality of life in children born prematurely.

**PRE-FEEDING SENSORIMOTOR INTERVENTIONS DECREASE THE
TRANSITION TIME TO INDEPENDENT ORAL FEEDING
IN PRETERM INFANTS**

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4.1 Abstract

Objectives: To assess whether a pre-feeding uni-oral (O), uni-tactile/kinesthetic (T/K) and multi-oral+tactile/kinesthetic (O+T/K) stimulation enhances preterm infants' oral feeding performance, and to delineate the impact of uni- versus multi-sensorimotor stimulation on oral feeding performance.

Study Design: Seventy-five preterm infants (26-32 weeks gestation) were randomized into four groups: the uni-O group involved sensorimotor input to the oral structures; the uni-T/K group received sensorimotor input to the head, neck, trunk, and limbs; the multi-O+T/K group involved O and T/K sensorimotor input, as above; and the control group. Outcomes included: time to attainment of independent oral feeding (days), proficiency (%), volume transfer (%), rate of transfer (ml/min), and volume loss (ml, spillage). Data were analyzed with one-way or repeated measures ANOVA.

Results: Independent oral feeding was achieved significantly earlier in all three intervention groups than the control group ($p < 0.001$). Proficiency and volume transfer were significantly greater in the three intervention groups, rate of transfer was significantly greater in the uni-O and multi-O+T/K groups, and there was less volume loss in the uni-O group only compared to the control group (all tests $p \leq 0.042$).

Conclusion: All three sensorimotor interventions improved preterm infants' oral feeding performance. Such findings support the notion that oral feeding performance can be improved by early training experiences that are tapping into distinct oral and non-oral sensorimotor systems.

4.2 Introduction

Up to 30% of preterm infants may encounter oral feeding difficulties, such as disorganized sucking pattern, uncoordinated suck-swallow-respiration, poor endurance, and oral hypersensitivity/aversion (Comrie & Helm, 1997; Harris, 1986; Hawdon et al., 2000; VandenBerg, 1990). These oral feeding difficulties are of concern to health care professionals because they often delay hospital discharge, negatively affect mother-infant bonding, and lead to childhood feeding disorders (Burklow et al., 2002; Hawdon et al., 2000; Schanler et al., 1999). The short- and long-term impact of neonatal oral feeding difficulties points to the critical need for more efficacious early interventions to facilitate the appropriate development of oral feeding skills in preterm infants (Burklow et al., 2002; Dodrill et al., 2004).

Sensorimotor stimulation is one type of early intervention. It is based on the theoretical framework that the in-utero environment provides all the necessary sensory stimulation for optimizing infants' developmental outcomes (Als, 1986, 1996; Korner, 1990). Preterm birth not only disrupts the normal developmental trajectory, but places infants in a highly technological environment. Although this technological environment is necessary for their survival, it exposes them to developmentally inappropriate stimuli, such as invasive medical procedures (e.g. suctioning of secretions, heel stick for blood sampling), bright lights, loud noises, decreased positive touch and prolonged separation from their mother (Als, 1986, 1996; Korner, 1990). Exposure to such factors at a time of rapid brain development may alter neuronal differentiation, and in turn may negatively influence later development (Als, 1986, 1996; Korner, 1990). Given that developmental impairments occur in infants with no history of brain insults exemplifies the impact

environmental influences have on brain development (Als, 1986, 1996). Therefore, provision of early positive sensorimotor stimulation, such as oral, tactile, kinesthetic, and/or vestibular, may promote appropriate neuronal organization leading to developmentally appropriate oral feeding skills (Hadders-Algra, 2000; Korner, 1990).

Safe and successful oral feeding is a highly complex process necessitating the appropriate function and interaction of multiple systems, including the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral, and neurological systems (Burklow et al., 2002; Hill, 2002; McGrath & Braescu, 2004; Ross & Browne, 2002; Thoyre, 2003). It is speculated that oral and non-oral sensorimotor stimulations may enhance the development of associated systems leading to improved oral feeding performance. Oral stimulation is the most commonly utilized sensorimotor intervention to improve preterm infants' oral feeding performance. Beneficial effects of a pre-feeding oral stimulation, prior to the start of oral feeding, on the nipple feeding performance of preterm infants are well documented (Fucile et al., 2002; 2005; Rocha et al., 2006). However, oral stimulation is aimed at improving the function of oral structures only. Limited information is available on the effect of non-oral sensorimotor interventions. There is evidence that tactile/kinesthetic stimulation consisting of stroking the head, neck, limbs, and torso, along with passive range of motion of the limbs may improve oral feeding performance by enhancing other systems, beyond oral-motor function. Specifically, tactile/kinesthetic stimulation has been found to advance motor development, promote alert behavioral states, increase gastrointestinal function, i.e. gastric motility, and improve weight gain (Diego et al., 2005; Dieter et al., 2003; Field et al., 1986; Mathai et al., 2001). Since these factors are also associated with oral feeding, it is likely that

tactile/kinesthetic stimulation may improve oral feeding performance. Indeed, Rausch (1981) and White & Labarba (1976) demonstrated that preterm infants who received 15 minutes of tactile/kinesthetic stimulation, 1-4 times a day, for 10 days had an increase in volume of milk ingested. However, these results are limited because the authors did not delineate whether the intake was via tube or oral feeding (Rausch, 1981), the trial was not randomized (White & Labarba, 1976), and there was no blinding during intervention (White & Labarba, 1976). Further studies are needed to clearly establish the effect of tactile/kinesthetic stimulation on preterm infants' oral feeding skills.

Uni-sensorimotor stimulations (one type of stimulation) may have beneficial effects beyond their targeted area, and thus may have favorable effects on multiple systems (Dieter & Emory, 1997; Korner, 1990). Accordingly, different types of uni-sensorimotor stimulation may have common beneficial outcomes. Therefore, it is conceivable that the simultaneous provision of multi-sensorimotor interventions (more than one type of stimulation), such as oral plus tactile/kinesthetic stimulations may have an additive or synergistic effect, leading to better oral feeding performance than a uni-sensorimotor intervention, i.e. oral or tactile/kinesthetic stimulation alone. This concept is partially supported by White-Traut et al., (2002) who demonstrated that a multi-stimulation intervention consisting of auditory, tactile, visual, and vestibular stimuli promoted alertness, accelerated the transition to complete nipple feeding and decreased length of hospitalization in preterm infants. However, this was a retrospective study and only a multi-stimulation intervention was provided, hence differentiation of additive or synergistic effects could not be determined. A prospective study with both uni- and multi-

sensorimotor interventions would establish the effect of multi-sensorimotor stimulations on the oral feeding performance of preterm infants more conclusively.

Taken together, the following hypotheses are proposed: 1) preterm infants who receive a pre-feeding uni-oral (O) stimulation, uni-tactile/kinesthetic (T/K) stimulation or multi-oral plus tactile/kinesthetic (O+T/K) stimulation, before the introduction of nipple feeding, will demonstrate improved oral feeding performance over those in the control group. More specifically, they will attain independent oral feeding sooner, demonstrate greater proficiency, volume transfer, rate of transfer, and have less volume loss (spillage) than controls; 2) preterm infants who receive a pre-feeding multi-O+T/K stimulation will demonstrate better oral feeding performances than those who receive uni-O or uni-T/K singly. The present study will provide new information on the influence of non-oral sensorimotor interventions on the oral feeding performance of preterm infants and establish the effect of uni- versus multi-sensorimotor stimulation interventions. Such information is necessary in order to provide the most appropriate and efficacious oral feeding intervention.

4.3 Methods

4.3.1 Participants

Eligibility was limited to clinically stable preterm infants, born between 26 and 32 weeks gestational age (GA), appropriate size for GA as determined by obstetric ultrasound and clinical examination, and receiving all tube feedings. Infants were excluded from the study if they had any congenital anomalies (e.g. oral or cardiac), and/or chronic medical complications, including severe bronchopulmonary dysplasia (BPD, Walsh et al., 2006), intraventricular hemorrhages (IVH) III or IV (Papile, Burstein,

Burstein, & Koffler, 1978), periventricular leukomalacia (PVL, de Vries, Eken, & Dubowitz, 1992), or necrotizing enterocolitis (NEC, Bell et al., 1978). All participants were recruited from the neonatal intensive care unit (NICU) at Texas Children's Hospital, Houston, TX, USA. The Institutional Review Board for Human Subject Research of Baylor College of Medicine and Affiliated Hospitals approved the research protocol.

4.3.2 Interventions

All participants received standard nursery care. In addition, infants in the uni-O stimulation group received 15 minutes of sensorimotor input to the peri- and intra-oral structures, twice a day. Specifically, the first 12 minutes consisted of stroking the cheeks, lips, gums and tongue and the final 3 minutes involved sucking on a pacifier, while infants were in supine position (Fucile et al., 2002). This protocol was selected because in an earlier study we found that it accelerated the transition to independent oral feeding, increased overall intake and rate of transfer (Fucile et al., 2002). Infants in the uni-T/K stimulation group received 15 minutes of sensorimotor input to the whole body, twice a day. It involved 10 minutes of stroking the head, neck, back, arms and legs in prone position, and 5 minutes of passive range of motion of the upper and lower limbs into flexion and extension in supine position (Field et al., 1986). This protocol was selected because it has been shown to have beneficial effects on preterm infants' motor development, behavioral state, and gastrointestinal function (Dieter et al., 2003; Field et al., 1987; Field et al., 1986; Mathai et al., 2001). Infants in the multi-O+T/K group received 15 minutes of O and 15 minutes of T/K stimulation as described above, each once a day, in random order. Infants in the control group did not receive any stimulation. Rather the researcher (SF) placed her hands in the isolette, but did not touch the infant for

15 minutes, twice a day. This particular protocol was designed to control for any possible effects of the daily presence of the researcher at the bedside. Moreover, no human touch was provided during the control intervention because static touch i.e. placing of hands on the infants' head and abdomen has been shown to decrease oxygen requirement and increase behavioral state organization in preterm infants 27-32 weeks gestation (Jay, 1982). Such benefits may in turn influence oral feeding performance.

4.3.3 Outcomes

The primary outcome measure was *time to attainment of independent oral feeding*, defined as the number of days to make the transition from all tube feeding to 8 successful oral feedings per day. Success was defined as the completion of the entire prescribed volume of milk without any occurrence of apnea, bradycardia or oxygen desaturation within the allotted 20 minutes.

The secondary outcomes included: *proficiency*, defined as the volume of milk transferred during the first 5 minutes over the prescribed volume to be taken (%); *volume transfer*, expressed as the volume of milk taken during an entire feeding session over the total prescribed volume (%); *rate of transfer*, described as the volume of milk transferred over the duration of the oral feeding session (ml/min); and *volume loss*, defined as the volume of milk spilled from the lips during the oral feeding, by subtracting the weight of the bib before from the weight after the feeding session (ml, this is based on the density of milk approximating 1 gram = 1 ml).

Time to attainment of independent oral feeding (days) was selected as the primary outcome measure because it is a criterion for hospital discharge (American Academy of Pediatrics, 1998). Proficiency, volume transfer, rate of transfer, and volume loss were

selected because they are indicators of specific oral feeding skills. Proficiency is an indicator of infants' nutritive sucking skill organization and ability to coordinate suck-swallow-respiration because it is monitored during the first 5 minutes of the oral feeding session when fatigue is presumed to be minimal (Case-Smith, 1989). Volume transfer reflects infants' overall nutritive sucking skill, as well as their suck-swallow-respiration coordination, endurance, and gastrointestinal function (defined as transport of food, digestion of food, absorption of nutrients, and eliminating waste). Rate of transfer is an indicator of infants' suck-swallow-respiration coordination efficiency and endurance. Volume loss is a marker of infants' oral muscular strength, i.e. lip seal. Such information can provide insight regarding the underlying mechanism mediating the effects of each intervention.

To ensure results were not biased, the following potential covariates were recorded: severity of illness using the Nursery Neurobiologic Risk Score (NBRS) which provides an overall score of infants' medical condition during their hospitalization (Brazy, Eckerman, Oehler, Goldstein, & O'Rand, 1991), number of infants who received all and/or partial breast feeding sessions and co-interventions (occupational, physical and/or speech therapy), and number of parental visits. As well, postmenstrual age (PMA), body weight, behavioral state at each 5 minute interval of the oral feeding session using a 3-point scale (1=sleep, 2= drowsy/awake, 3=fussy/crying), and episodes of apnea (cessation of breathing for ≥ 20 seconds), bradycardia (heart beat < 100 for 10 seconds) and/or oxygen desaturation (oxygen saturation $< 85\%$) at the three monitored oral feeding sessions were recorded. To make certain results were not influenced by a possible Hawthorne effect, such as the supplementary daily presence of a research person at the

bedside, data on the primary outcome were gathered over the same study period by chart review for 10 additional infants who received standard nursery care, named the 'Hawthorne group'.

4.3.4 Procedures

Approval to approach parents was obtained from the attending neonatologist. Informed parental consent was then obtained before participants entered the study. All infants were randomized into a uni-O, uni-T/K, multi-O+T/K, or control group using a stratified blocked randomization. Stratification by GA (26-29 vs. 30-32 weeks GA) was used to ensure that the four groups had equal GA distribution, and also stratification by time (per 3 months) to make certain each group had similar distribution of attending neonatologists.

The uni-O, uni-T/K, multi-O+T/K, and control interventions were commenced 48 hours after discontinuation of nasal continuous positive airway pressure. Infants were either on room air or on nasal cannula. All interventions were administered in two 15-minute sessions per day (30 minutes/day), for a total of 10 days within a 14-day period. The two daily sessions were provided, 15 to 30 minutes before tube feedings in the morning and afternoon, with at least a 3-hour interval between each session. The choice of this regimen was based on studies using O or T/K stimulation which demonstrated that 15 minutes of either sensorimotor stimulation 1 to 4 times per day, prior to tube feeding, led to positive effects on oral feeding performance, gastrointestinal function, and behavioral state (Field et al., 1986; Fucile et al., 2002; White & Labarba, 1976; White-Traut et al., 2002). Interventions were not provided if infants had an increased oxygen requirement within the last 24 hours, increased occurrence of apnea/bradycardia or

oxygen desaturation within the last 24 hours, and if there was a major disruption 30 minutes prior to the start of the stimulation, such as ophthalmologic examination, based on nurses' or attending neonatologists' recommendation and chart review. Infants' responses were closely monitored for signs of distress throughout the interventions. The sessions were stopped if infants presented with any one of the following signs of distress: apnea, bradycardia, oxygen desaturation, fussing (denoted by splaying arms and legs), crying, and vomiting/spitting up. All interventions were provided at the bedside. A screen was placed around the infants' isolette so as to blind caretakers and family members to group assignment. The researcher (SF), specialized in NICU care, was responsible for administration of all the interventions. Infection control procedures implemented by the hospital were followed during the interventions, such as stringent hand washing and wearing a hospital gown prior to each intervention.

All participants were monitored from the start of the study (i.e. when the sensorimotor stimulation was commenced) to hospital discharge. The initiation and advancement of oral feedings was left to the sole discretion of the attending physician. The nurses were responsible for feeding infants in their customary way, with no encouragement, e.g. chin and/or cheek support during the monitored oral feeding sessions. Both neonatologists and nurses were blind to group assignment. The outcome variables were measured at specific times throughout the study. Time to attainment of independent oral feeding was defined as the first time an infant reached 8 successful oral feedings/day, for 2 consecutive days. Proficiency, volume transfer, rate of transfer, and volume loss were monitored during 3 oral feeding sessions, once when infants were taking 1-2, 3-5, and 6-8 oral feedings/day.

4.3.5 Statistical Analyses

One-way ANOVA was used to determine the effect of each intervention on time to attain independent oral feeding. A repeated measures ANOVA was used to compare the effect of the interventions on proficiency, volume transfer, rate of transfer, and volume loss over time. In cases of statistical significance post-hoc Bonferroni tests were used to assess differences between groups and time. For the purpose of this study, post-hoc group and time effects were analyzed, but post-hoc group by time interaction effects were not analyzed because the clinical significance is marginal and further analyses would not add more to our understanding of the underlying mechanism of each intervention. Oral feeding performance outcomes were first analyzed by stratifying GA into 2 groups, 26-29 and 30-32 weeks GA. No significant differences were found and all subsequent analyses were performed on the pooled sample (26-30 weeks GA). Significance was defined at the 0.05 level. Analyses were performed using the Statistical Program for Social Sciences software version 15.0 (SPSS, Inc., Chicago, IL).

Sample size was calculated based on a type 1 error of 0.05 and a power of 0.80. Sample size estimation was derived from the primary outcome, time to attainment of independent oral feeding, which at Texas Children's Hospital averaged 14 ± 8 days (Fucile et al., 2002). A decrease of 8 days (1 SD) to attain independent oral feeding was considered a clinically important effect. Thus, a sample size of 64 (16 participants per group) was needed. However, an additional 30% of infants were enrolled to allow for infants who may develop serious medical illnesses, and would be too fragile to complete the study. These would be infants who had their tube or oral feedings stopped for greater

than 7 consecutive days, developed severe BPD, IVH III or IV, PVL, and NEC after the start of the study. Therefore, 84 participants (21 infants per group) were recruited.

4.4 Results

4.4.1 Participants

Eighty-four participants were enrolled. After enrollment, 4 infants were transferred to another hospital, 4 developed NEC and 1 had a congenital heart defect. These conditions were diagnosed prior to the onset of the study. Therefore, a total of 75 infants completed the study. Infants in all 4 groups were comparable with regard to baseline characteristics, with the exception of ethnic distribution (Table 1). The ethnic distribution was reflective of Harris County, the location of Texas Children's Hospital, Houston, TX. All covariates were equally distributed between the 4 groups (all tests $p \geq 0.066$, Table 2).

4.4.2 Oral feeding performance

All 4 groups were introduced to oral feeding at similar PMA, days of life, and weight (Table 3). Infants in the uni-O, uni-T/K and multi-O+T/K groups achieved independent oral feeding sooner than the control group (all tests $p < 0.001$). However, there was no difference in time to attainment of independent oral feeding between the 3 experimental groups (all tests $p \geq 0.795$). Infants in the multi-O+T/K group attained independent oral feeding at a significantly younger PMA than the controls ($p = 0.020$). There was no difference in mean number of days to attain independent oral feeding between the Hawthorne group (19.8 ± 8.9) and the control group (20.7 ± 6.6 , $p = 1.000$).

The proficiency analysis (Figure 1) indicated a significant group effect ($F_{2, 35} = 7.213$, $p = 0.001$), time effect ($F_{2, 30} = 5.119$, $p = 0.012$), and group x time interaction ($F_{6, 35} = 7.213$, $p = 0.001$), time effect ($F_{2, 30} = 5.119$, $p = 0.012$), and group x time interaction ($F_{6, 35} = 7.213$, $p = 0.001$).

$_{60}=3.872$, $p=0.002$). Post-hoc Bonferroni tests indicated that the 3 experimental groups had significantly greater proficiency than the controls (all tests $p\leq 0.034$). However, proficiency did not differ between the 3 experimental groups (all tests $p=1.000$). On the time component, there was a significant increase in proficiency at 1-2, 3-5 and 6-8 oral feedings/day (all tests $p\leq 0.049$).

In volume transfer (Figure 2), there was a significant group effect ($F_{3,42}=13.308$, $p<0.001$), time effect ($F_{2,30}=29.355$, $p<0.001$), and group x time interaction ($F_{5,89}=3.121$, $p=0.008$). Post-hoc Bonferroni tests indicated that the 3 experimental groups had significantly greater volume transfer than the control group (all tests $p\leq 0.007$). However, there was no difference in volume transfer between any of the 3 experimental groups (all tests $p=1.000$). The time component reflects a significant progression in volume transfer from 1-2, 3-5, and 6-8 oral feedings/day (all tests $p\leq 0.037$).

The rate of transfer analysis (Figure 3) indicated that there was a significant group effect ($F_{3,37}=3.264$, $p=0.003$), time effect ($F_{2,29}=13.534$, $p=0.001$), but no significant group x time interaction ($F_{4,55}=1.222$, $p=0.647$). Post-hoc Bonferroni tests indicated that the uni-O and multi-O+T/K group had a faster rate of transfer than the control group (all tests $p\leq 0.034$). There was no difference between the uni-T/K and control group nor between the 3 experimental groups (all tests $p\leq 0.332$). On the time component, there was a significant increase in rate of transfer from 1-2, 3-5, and 6-8 oral feedings/day (all tests $p\leq 0.017$).

In volume loss (Figure 4), there was a significant group effect ($F_{2,28}=6.173$, $p=0.007$), but no time effect ($F_{2,22}=1.824$, $p=0.190$), and no group x time interaction ($F_{5,71}=2.189$, $p=0.068$). Of the 3 experimental groups, post-hoc Bonferroni tests indicated

that the uni-O group was the only one with significantly less volume loss than the control group ($p=0.042$).

4.4.3 Sensorimotor stimulations

Table 4 illustrates that only 13 (1.1%) out of 1100 administered sensorimotor stimulations were stopped because of signs of distress, specifically occurrence of apnea, bradycardia or oxygen desaturation, which all resolved spontaneously. No stimulations were stopped because of fussing, crying, or vomiting/spitting up behaviors. There was no difference in mean number of days from the end of sensorimotor intervention period to the start of oral feeding between the 4 groups. Mean PMA, days of life, and weight when the sensorimotor stimulations were started and completed did not differ between the 4 groups (all tests $p \geq 0.072$).

4.5 Discussion

The aims of this study were to assess the efficacy of a pre-feeding uni-O, uni-T/K, and multi-O+T/K intervention on preterm infants' oral feeding performance, and to compare the effect of uni- versus multi-sensorimotor stimulations. Results indicate that both oral and non-oral sensorimotor stimulations i.e. uni-O, uni-T/K, and multi-O+T/K improved oral feeding performance compared to controls. However, the multi-O+T/K intervention did not lead to better oral feeding performance than the uni-O or uni-T/K sensorimotor stimulations.

4.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions

Infants in the 3 experimental groups attained independent oral feeding up to 10 days faster than those in the control group. All 4 groups were introduced to oral feeding at similar PMA, days of life, and body weights, and had similar health and baseline

characteristics eliminating the possibility that infants in the experimental groups attained independent oral feeding faster because they were more mature or in better health than those in the control group. The faster progression to independent oral feeding could not be due to a Hawthorne effect because of the lack of difference between the Hawthorne and control group.

Advancement of oral feeding is often based on infants' oral feeding performance, such as volume of milk intake (Premji et al., 2004; Shaker, 1999). Proficiency and rate of transfer have been suggested as potential indicators of volume transfer (Lau & Schanler, 1996). Hence, we attribute the more rapid transition to independent oral feeding observed in this study to improved proficiency, volume transfer and rate of transfer in the experimental groups. Specifically, all three experimental groups had improved proficiency and more volume transfer over the controls, the uni-O and multi-O+T/K groups had greater rate of transfer than the control group, and the uni-O group had less volume loss compared to the controls.

The finding that uni-O and uni-T/K, two distinct interventions, improved oral feeding performance compared to controls supports the notion that oral feeding is an integrated multiple systems process that may be enhanced by early training experiences which focus on oral as well as non-oral sensorimotor input. Several authors have suggested that well-defined sensorimotor interventions can have a positive effect through active training of specific developmental skills (Hadders-Algra, 2000; Korner, 1990). This is supported by our present observation as uni-O or uni-T/K stimulation tap into specific and distinct sensorimotor systems.

The uni-O stimulation, which targets the oral structures, improves nutritive sucking skills, in particular expression amplitude (Fucile et al., 2005). This improved nutritive sucking skill likely contributed to the greater proficiency, volume transfer, rate of transfer, and less volume loss in the uni-O group compared to controls, as strength of suck and sucking pattern were found to be correlated with oral feeding performance (Lau et al., 2000; Tamura, Matsushita, Shinoda, & Yoshida, 1998). It is plausible that uni-O stimulation not only improved the oral muscular function, but also ameliorated gastrointestinal function and cardio-respiratory function leading to better proficiency, volume transfer and rate of transfer. This speculation is based on the studies of Bernbaum et al., (1983) who found that non-nutritive sucking increases gastrointestinal transit time, and on Anderson & Vidyasagar (1979) who noted that non-nutritive sucking may facilitate gaseous exchange by increasing vascular perfusion to the parenchyma and tissue cells in the lungs. Such improvements in gastrointestinal and cardio-respiratory functions may increase infants' acceptance of greater volumes of milk and facilitate suck-swallow-respiration coordination, respectively leading to improved oral feeding performance.

The uni-T/K stimulation which targeted the head, neck, trunk and limbs also enhanced proficiency and volume transfer compared to the control. This improvement is possibly a result of better motor function, associated with tactile/kinesthetic stimulation. Studies have shown that tactile/kinesthetic stimulation increases motor activity, such as limb movement and muscle tone in preterm infants (Field et al., 1986; Scafidi et al., 1993; Vickers, Ohlsson, Lacy, & Horsley, 2004). This increased motor activity may in turn facilitate appropriate postural alignment providing a more stable base for sucking,

swallowing, and respiration (Redstone & West, 2004; Shaker, 1990). The increased volume transfer may also be mediated by improved gastrointestinal function. Specifically, tactile/kinesthetic stimulation has been found to increase vagal tone/activity which in turn improves gastric motility (Diego et al., 2005). This enhanced gastric motility may allow for greater acceptance of milk volume during oral feeding as observed by White & Labarbe (1976). The improved proficiency and volume transfer may also be due to enhanced cardio-respiratory function. Kuhn et al., (1991) found that tactile/kinesthetic stimulation increased urinary levels of norepinephrine and epinephrine. These hormones mediate lung maturation and maintain cardiovascular homeostasis (Kuhn et al., 1991), potentially facilitating suck-swallow-respiration coordination. Although both proficiency and volume transfer were enhanced by uni-T/K stimulation compared to controls, rate of transfer and volume loss did not differ between these two groups. The lack of difference may be due to the fact that uni-T/K did not directly stimulate the oral structures. Thus, infants' oral musculature may not have been efficient and strong enough to sustain a maximal rate of transfer and a tight lip seal around the nipple.

The multi-O+T/K stimulation led to a more rapid transition to independent oral feeding as well as greater proficiency, volume transfer, and rate of transfer compared to the control. The finding that infants in the multi-O+T/K group were younger, as measured by PMA, than those in the control group at 8 successful oral feedings/day, further supports the notion that oral feeding performances were improved as a result of early oral and non-oral experiences rather than by maturation alone.

4.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions

Although multi-O+T/K stimulation was sufficient to lead to better oral feeding performance compared to controls, it did not result in additive or synergistic beneficial effects in comparison with the uni-O or uni-T/K interventions. The lack of an additive or synergistic beneficial effect may be related to the shorter duration of the stimulation because the multi-O+T/K stimulation consisted of 15 rather than 30 minutes of each mode. It is also probable that the lack of additive or synergistic effect may be due to the neuro-physiological status of the infant. In an earlier study we found that 15 minutes/day of uni-O stimulation accelerated the transition to independent oral feeding by a mean of 8 days (Fucile et al., 2002), which is similar to the mean of 9 days with 30 minutes/day of uni-O stimulation in this study. These findings suggest that there may be a limit to the extent to which preterm infants can respond to sensorimotor input which may be dependent on their neurological state of development (Hadders-Algra, 2000; Korner, 1990). For example, during oral feeding respiration is disrupted with each swallow, resulting in a decrease in minute ventilation and oxygenation (Mathew, 1991; Shivpuri et al., 1983; Wilson et al., 1981). If these respiratory limits are exceeded apnea, bradycardia and oxygen desaturation may occur (Mathew, 1991; Shivpuri et al., 1983). The limit to respond may be reached when the suck-swallow-respiration cycle is compromised. Hence, there may be a ceiling on the extent to which sensorimotor interventions may advance oral feeding performance that is determined by the level of neural integrity and controls associated with the suck-swallow-respiration cycle. In support of this, several authors have stated that sensorimotor input is effective on emerging or developing systems (Hadders-Algra, 2000; Korner, 1990). A dose response study would shed light

on the optimal response to sensorimotor interventions of preterm infants' oral feeding performance.

4.6 Conclusion

This study supports the notion that oral feeding performance may be improved by early training experiences tapping into distinct sensorimotor systems. The data demonstrate that oral feeding performance of preterm infants may be enhanced by both oral and non-oral sensorimotor interventions. Diverse underlying mechanisms appear to mediate the beneficial effects of oral and tactile/kinesthetic stimulations. Multi-sensorimotor stimulations, as implemented here, do not have an additive or synergistic effect on oral feeding performance. It is proposed that there seems to be an upper limit for advancing oral feeding performance, determined by the neuro-developmental state of preterm infants. Given our current understanding of the time limits for stimulation, we advocate that pre-feeding oral and non-oral sensorimotor interventions be implemented in neonatal developmental care plans taking these limits into consideration.

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4.8 References

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4.9 Tables and figures

Table 1: Baseline characteristics of preterm infants in the 4 study groups

	Uni-Oral (n=19)	Uni-Tactile/ Kinesthetic (n=18)	Multi- O+T/K (n=18)	Control (n=20)	<i>P</i> [†]
Gestational age (wks)	29.6 ± 1.5	29.1 ± 2.0	29.0 ± 1.8	29.4 ± 1.9	0.689
Infant distribution					
26-29 weeks	10	8	11	9	0.266 [‡]
30-32 weeks	9	10	7	11	
Birth weight (g)	1359.7 ± 341.1	1325.4 ± 324.7	1329.6 ± 293.0	1346.6 ± 358.3	0.988
Gender distribution					
Male	12	11	10	16	0.057 [‡]
Female	7	7	8	4	
Apgar score (5 min)	8.1 ± 0.4	8.5 ± 0.5	8.3 ± 0.7	8.3 ± 0.5	0.089
Ethnic Distribution					
African American	8	3	4	5	0.010 [‡]
Caucasian	6	4	9	3	
Hispanic	5	11	5	12	

Data presented as means ± SD or number of participants, [†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

Table 2: Covariate distribution between the 4 study groups

	Uni-Oral	Uni-Tactile/ Kinesthetic	Multi- O+T/K	Control	P†
Severity of illness					
(NBRS)	2.6 ± 1.4	2.4 ± 1.6	2.3 ± 1.4	2.5 ± 1.7	0.916
No. infants who had					
breastfeeding	4	8	5	6	0.241‡
No. infants who had					
co-interventions	10	15	13	14	0.117‡
No. parental visits	18.6 ± 11.3	21.8 ± 13.4	21.6 ± 10.8	24.3 ± 14.2	0.577
1-2 PO/day					
PMA (wks)	34.4 ± 1.5	34.4 ± 1.7	34.0 ± 1.1	34.2 ± 1.5	0.716
Weight (g)	2058.7 ± 355.7	2179.6 ± 440.9	2069.9 ± 228.5	2013.9 ± 277.1	0.485
Behavior state	2	2	2	2	0.409‡
No. infants a/b/o ₂	1	3	0	4	0.155‡
3-5 PO/day					
PMA (wks)	35.4 ± 1.6	36.6 ± 6.4	35.4 ± 5.1	35.9 ± 1.8	0.823
Weight (g)	2246.5 ± 288.5	2367.2 ± 463.4	2213.6 ± 239.4	2250.6 ± 289.3	0.529
Behavior state	2	2	2	2	0.985‡
No. infants a/b/o ₂	2	1	2	3	0.629‡
6-8 PO/day					
PMA (wks)	37.1 ± 3.9	35.9 ± 1.9	36.2 ± 4.3	36.6 ± 2.1	0.681
Weight (g)	2403.4 ± 278.9	2527.8 ± 436.8	2335.6 ± 297.0	2481.9 ± 376.0	0.372
Behavior state	2	2	2	2	0.510‡
No. infants a/b/o ₂	0	2	0	2	0.247‡

NBRS-nursery neurobiologic risk score, No.-number, PO-oral feedings/day, PMA-postmenstrual age, a/b/o₂-apnea/bradycardia/oxygen desaturation episodes, Data presented as means ± SD or number of participants, †One-way ANOVA unless otherwise indicated, ‡Fisher's exact test

Table 3: Number of days to make the transition to independent oral feeding

	Uni-Oral	Uni-Tactile/ Kinesthetic	Multi- O+T/K	Control	<i>P</i> †
Introduction to					
oral feeding					
PMA (wks)	34.2 ± 1.5	34.1 ± 1.7	33.2 ± 1.4	33.8 ± 1.4	0.197
DOL (days)	33.8 ± 16.5	36.6 ± 22.3	30.4 ± 13.5	30.4 ± 16.6	0.659
Weight (g)	2001.3 ± 276.0	2065.6 ± 461.0	1952.1 ± 206.8	1885.2 ± 282.3	0.361
Independent					
oral feeding					
Number of days	11.1 ± 3.5*	11.4 ± 3.3*	10.0 ± 3.5*	20.7 ± 6.6	0.000
PMA (wks)	35.9 ± 1.6	35.4 ± 1.9	34.7 ± 1.2*	36.2 ± 1.6	0.020
DOL (days)	44.7 ± 16.1	46.5 ± 21.8	40.1 ± 12.8	49.3 ± 21.3	0.487
Weight (g)	2345.8 ± 292.4	2442.0 ± 438.5	2305.7 ± 254.5	2465.8 ± 390.2	0.454

PMA-postmenstrual age, DOL-days of life, Data presented as means ± SD, †One-way ANOVA, Post-hoc Bonferroni tests **p* ≤ 0.05 vs. control

Table 4: Features of the sensorimotor stimulations

	Uni-Oral	Uni-Tactile/ Kinesthetic	Multi- O+T/K	Control	<i>P</i> [†]
Start					
stimulation					
PMA (wks)	32.7± 0.9	32.1 ± 1.2	31.7 ± 1.6	32.5 ± 1.4	0.079
DOL (days)	23.4± 16.4	24.3± 17.5	19.6 ± 15.0	23.0± 18.2	0.851
Weight (g)	1676.3 ± 281.0	1673.4 ± 236.2	1615.8 ± 287.1	1709.5 ± 236.9	0.742
End					
stimulation					
PMA (wks)	34.3± 1.3	33.6 ± 1.2	33.1 ± 1.5	34.0 ± 1.2	0.072
DOL (days)	33.8± 16.5	35.1 ± 17.2	30.3 ± 14.7	33.6 ± 18.2	0.854
Weight (g)	1987.4 ± 291.7	1994.2 ± 299.5	1905.0 ± 318.8	2000.0 ± 291.6	0.749
No. days					
from end stim.	3.5 ± 4.4	3.1 ± 4.1	3.9 ± 3.8	3.2 ± 3.3	0.782
to start PO					
Signs of distress	4	4	5	N/A	0.205 [‡]

PMA-postmenstrual age, DOL-days of life, Stim-stimulation, No-number, PO-oral feeding,
 Data presented as means ± SD or number of participants, [†]One-way ANOVA unless otherwise indicated,
[‡]Fisher's exact test

Figure 1: Proficiency (%) at the three monitored oral feeding sessions.

Data presented as means \pm SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in proficiency between the three intervention groups and the control group (all tests $p \leq 0.034$), and a significant increase in proficiency over time (all tests $p \leq 0.049$).

Figure 1

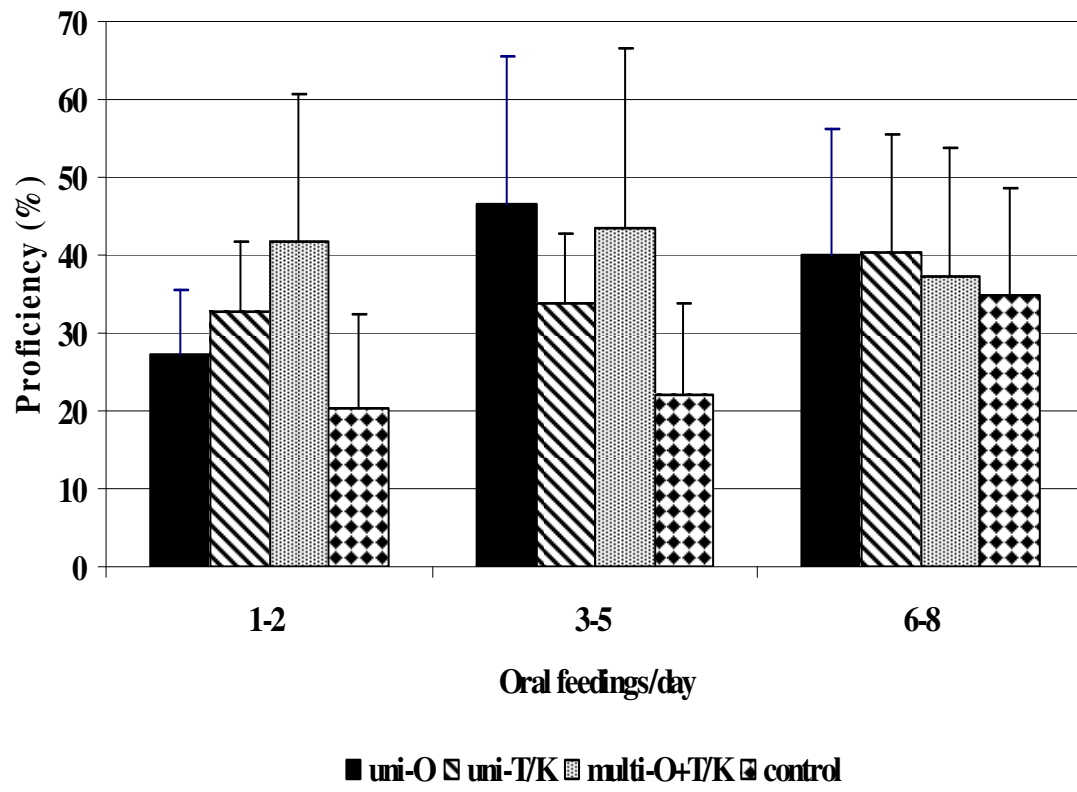


Figure 2: Volume transfer (%) at the three monitored oral feeding sessions.

Data presented as means \pm SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in volume transfer between the uni-O, uni-T/K, multi-O+T/K and controls (all tests $p \leq 0.007$), and a significant increase in volume transfer over time (all tests $p \leq 0.037$).

Figure 2

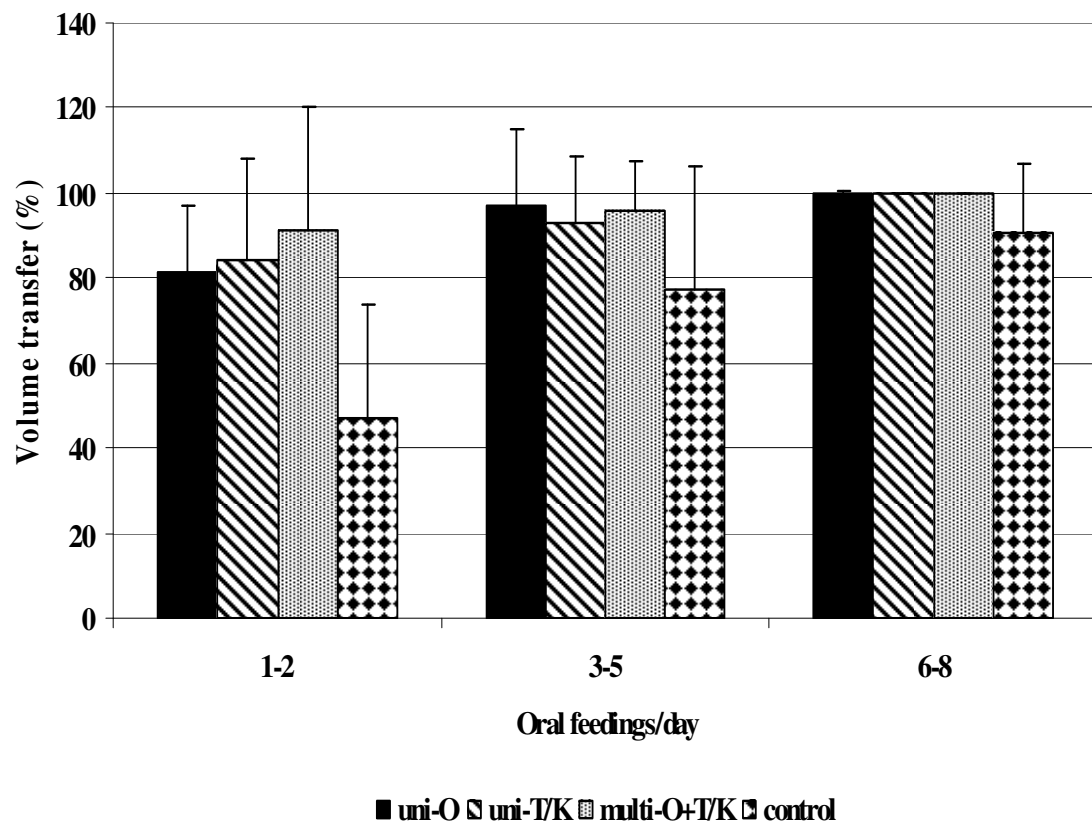


Figure 3: Rate of transfer (ml/min) at the three monitored oral feeding sessions.

Data presented as means \pm SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in rate of transfer between the uni-O and multi-O+T/K and the controls (all tests $p \leq 0.034$), and a significant increase in rate of transfer over time (all tests $p \leq 0.017$).

Figure 3:

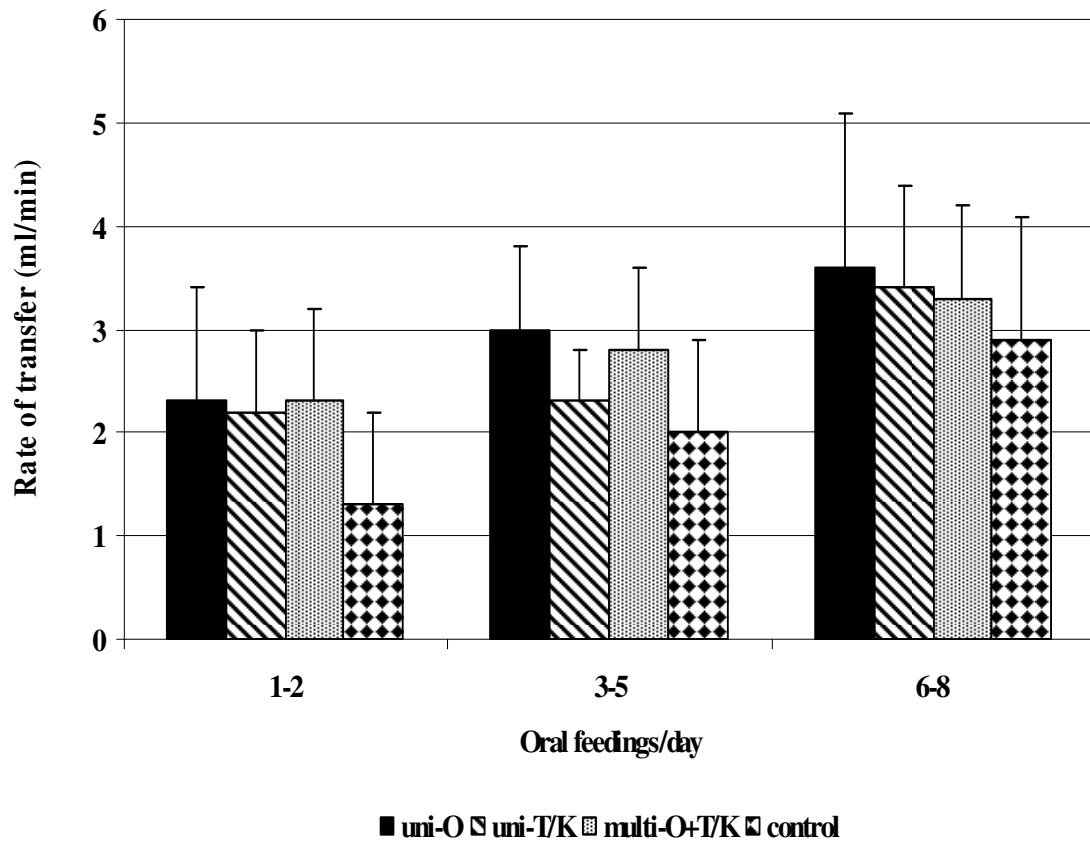
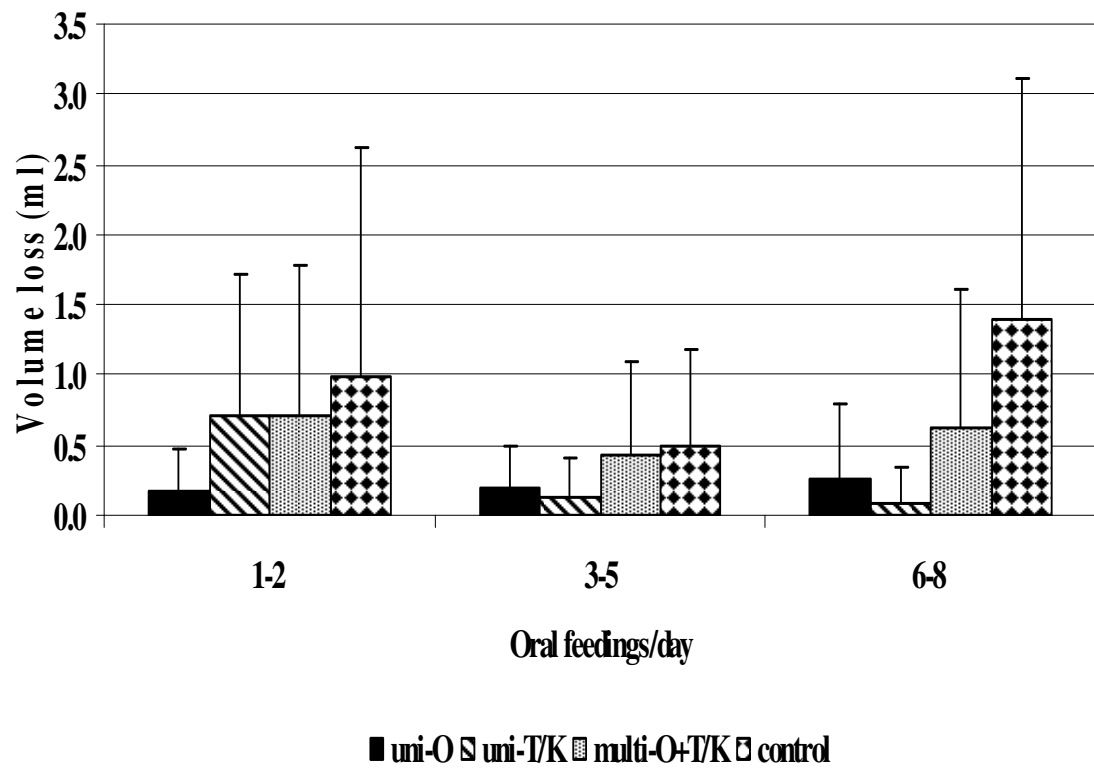


Figure 4: Volume loss (ml) at the three monitored oral feeding sessions.

Data presented as means \pm SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in volume loss between the uni-O and the control group only ($p=0.042$).

Figure 4:



CHAPTER 5

INTRODUCTION TO MANUSCRIPT 2

“PRE-FEEDING SENSORIMOTOR INTERVENTIONS PROMOTE NUTRITIVE SUCKING SKILLS IN PRETERM INFANTS”

The findings from the first manuscript demonstrate that uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations enhanced preterm infants' oral feeding performance (Fucile, Gisell, & Lau, 2008). Specifically, all three sensorimotor interventions accelerated the transition to independent oral feeding compared to controls. The uni-oral and multi-oral + tactile/kinesthetic stimulations improved proficiency, volume transfer, and rate of transfer, the uni-tactile/kinesthetic stimulation increased proficiency and volume transfer, and only the uni-oral stimulation led to a decrease in volume loss (spillage) compared to controls (Fucile et al., 2008). The multi-oral + tactile/kinesthetic stimulation did not lead to additive or synergistic beneficial effects, rather all three experimental groups improved oral feeding performance to the same extent.

Knowledge on the underlying mechanisms mediating the improved oral feeding performance is very limited. It is proposed that advanced nutritive sucking skills, such as stage of sucking, sucking burst duration, sucking rate, and suction and expression amplitudes may have contributed to this improved oral feeding performance. Indeed, we found in an earlier study that oral stimulation enhanced the amplitude of the expression component of sucking (Fucile et al., 2005). Whether increased duration of oral stimulation may further enhance nutritive sucking skills remains unknown. Moreover, the

impact of uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations on preterm infants' nutritive sucking skills has not been investigated. It is postulated that uni-tactile/kinesthetic stimulation may facilitate nutritive sucking by increasing infants' neck and trunk stability allowing for a more stable base to generate sucking (Bosma, 1973; Comrie & Helm, 1997; Redstone & West, 2004). Therefore, simultaneous provision of both oral and tactile/kinesthetic interventions may lead to additive or synergistic beneficial effects on preterm infants' nutritive sucking skills. Further studies are needed to assess and compare the effect of uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic interventions on the nutritive sucking skills of preterm infants.

Therefore, this second manuscript, examines the impact of uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations on the nutritive sucking skills of preterm infants. The same group of infants as in manuscript one was examined. Potential confounders which may influence nutritive sucking skills were taken into consideration. We assessed the impact of each intervention on infants' nutritive sucking skills, specifically stages of sucking, sucking burst duration, sucking rate, and suction and expression amplitudes as they progressed from all tube to independent oral feeding. Results from this study will allow us to gain a better understanding of the underlying nutritive sucking skills that may have contributed to the observed oral feeding improvements in the three experimental groups. Increased knowledge about the nature of sensorimotor interventions will also allow us to provide more specific and more efficacious pre-feeding sensorimotor interventions aimed at facilitating appropriate development of nutritive sucking skills, and thereby minimizing oral feeding difficulties in this high risk group.

**PRE-FEEDING SENSORIMOTOR INTERVENTIONS PROMOTE NUTRITIVE
SUCKING SKILLS IN PRETERM INFANTS**

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5.1 Abstract

The aims of this study were to assess the effect of a pre-feeding uni-oral (O), uni-tactile/kinesthetic (T/K), and multi-O+T/K stimulation on preterm infants' nutritive sucking skills and to delineate the influence of uni- versus multi-sensorimotor interventions on nutritive sucking skills. Seventy-five infants (mean age 29 [1.8 SD] weeks gestation, 49 males/26 females) were randomly assigned to a uni-O group involving sensorimotor input to the oral structures; a uni-T/K group involving sensorimotor input to the body and limbs; a multi-O+T/K group consisting of the same O and T/K stimulations as above; and a control group. The uni-O group had significantly more advanced stages of sucking as well as greater suction and expression amplitudes than the control group (all tests $p \leq 0.035$). As well, the uni-O group had greater expression and suction amplitudes than the uni-T/K and multi-O+T/K groups, respectively (all tests $p \leq 0.035$). Oral stimulation was the only intervention to significantly enhance nutritive sucking skills. Results demonstrate that development of nutritive sucking skills may be influenced by early sensorimotor interventions that specifically target the oral musculature involved in the generation of nutritive sucking.

5.2 Introduction

Preterm infants face several challenges for successful oral feeding, such as immature sucking skills, a disorganized sucking pattern, and inability to coordinate sucking, swallowing and respiration (White-Traut et al., 2005). Such difficulties interfere with infants' ability to achieve independent oral feeding, thereby prolonging their hospital stay (Bazyk, 1990; Burklow et al., 2002; Schanler et al., 1999). Present cost containment efforts necessitate hospital discharge of preterm infants at the earliest possible time (McGrath & Braescu, 2004). Hence, early intervention strategies that facilitate the proper acquisition of sucking, swallowing, and respiration are needed to prevent or reduce oral feeding difficulties in this high risk group (Burklow et al., 2002).

Introduction and advancement of oral feeding is based primarily on the competence of infants to feed safely and successfully. Safe and successful oral feeding is defined as an infant's ability to take the entire prescribed volume of milk by mouth, within an appropriate amount of time, with no adverse clinical events, such as apnea, bradycardia, and oxygen desaturation (Simpson et al., 2002). The generation and coordination of sucking, swallowing, and respiration is essential in achieving this milestone (Bu'Lock et al., 1990). During nutritive sucking, the bolus of milk is obtained from the alternation of suction and/or expression components or the expression component only (Dubignon & Campbell, 1969; Lau et al., 2000; Sameroff, 1968). Suction is the negative intra-oral pressure created by lowering the jaw and tongue to draw milk from the nipple (Colley & Creamer, 1958; Dubignon & Campbell, 1969). Expression is the stripping/compression of the nipple between the tongue and the hard palate to eject the milk from the nipple (Ardran et al., 1958; Dubignon & Campbell,

1969). Once the bolus is formed, it is carried to the pharynx by peristaltic motions of the tongue (Arvedson & Lefton-Greif, 1998). As the bolus is collected posteriorly, a swallow is initiated and respiration is interrupted during this process (Arvedson & Lefton-Greif, 1998).

Preterm infants' underdeveloped and/or disorganized sucking pattern is one of the main factors impeding their transition from tube to oral feeding (Pickler, Best, Reyna, Gutcher, & Wetzel, 2006). Lau et al. (2000) described the development of nutritive sucking in infants born less than 30 weeks gestation, by classifying their sucking pattern into 5 developmental stages, based on the presence/absence and rhythmic alternation of suction and expression components. Stage 1, represents an immature/disorganized sucking pattern characterized by no suction, arrhythmic expression, and/or arrhythmic alternation of suction/expression. Stage 2, 3 and 4 represent maturing sucking patterns, with suction emerging, more rhythmic expression, and/or more rhythmic alternation of suction and expression. Stage 5, represents a mature sucking pattern with well-defined and rhythmic presence of suction and expression, similar to that of full term infants. A mature sucking pattern is not necessary to attain safe and successful oral feeding (Lau et al., 1997). However, there is a significant positive correlation between stages of sucking and both overall milk intake and rate of milk transfer, suggesting that the maturation of sucking skills plays a significant role in improving oral feeding performance (Lau et al., 2000).

Preterm infants' nutritive sucking difficulties and their subsequent influence on ability to orally feed makes it imperative to develop cost effective early interventions that can facilitate the acquisition of nutritive sucking skills (Burklow et al., 2002). In an

earlier study, we demonstrated that a pre-feeding uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic sensorimotor intervention, administered prior to the start of oral feeding, accelerated the transition from tube to oral feeding by 9-10 days. The uni-oral and multi-oral + tactile/kinesthetic stimulations improved proficiency (volume taken in first 5 minutes/prescribed volume, %), volume transfer (volume taken over the entire feeding session/prescribed volume, %), and rate of transfer (ml/min), the uni-tactile/kinesthetic stimulation increased proficiency and volume transfer, and only the uni-oral stimulation led to a decrease in volume loss (spillage) compared to controls (Fucile et al., 2008). These oral feeding performances are indicators of infants' oral feeding skills, such as nutritive sucking. Hence, it is likely that such improved oral feeding performances are due to enhanced nutritive sucking skills. Indeed, 15 minutes of oral stimulation was found to increase the amplitude of the expression component of nutritive sucking (Fucile et al., 2005). Whether longer than 15 minutes of oral stimulation may further enhance nutritive skills remains unknown. Moreover, the impact of uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations on preterm infants' nutritive sucking skills has not been investigated. It is likely that tactile/kinesthetic stimulation involving sensorimotor input to neck, trunk, and limbs may also facilitate nutritive sucking by increasing infants' neck and trunk stability, thereby providing a more stable base for the generation of sucking (Bosma, 1973; Comrie & Helm, 1997; Redstone & West, 2004). Therefore, simultaneous provision of both oral and tactile/kinesthetic interventions may lead to additive or synergistic beneficial effects on preterm infants' nutritive sucking skills.

Based on the above, the following hypotheses are proposed: 1) preterm infants who receive a pre-feeding uni-oral (O), uni-tactile/kinesthetic (T/K), or multi-O+T/K stimulation, before the introduction of oral feeding, will demonstrate more advanced nutritive sucking skills than those in the control group. More specifically, they will exhibit more mature stages of sucking, longer sucking bursts, faster sucking rates, and greater suction and expression amplitudes than controls; and 2) preterm infants who receive a multi-O+T/K stimulation will demonstrate more advanced nutritive sucking skills than those who receive a uni-O or uni-T/K stimulation alone. The findings from this study will provide a better understanding of the effects of sensorimotor interventions on preterm infants' nutritive sucking skills, and establish the influence of uni- versus multi-sensorimotor interventions. A more in-depth understanding of the impact of sensorimotor interventions is necessary in order to provide more specific early interventions to facilitate the appropriate development of nutritive sucking skills in this high risk group.

5.3 Methods

5.3.1 Participants

All participants were recruited from the neonatal intensive care unit at Texas Children's Hospital, Houston, TX, USA. The study was approved by the Institutional Review Board for Human Subjects at Baylor College of Medicine and Affiliated Hospitals. Informed parental consent was obtained prior to subjects' entry into the study, following consultation with the attending physician.

To be eligible infants had to be: 1) born between 26-32 weeks gestational age (GA), as determined by obstetric ultrasound and clinical examination. In instances where

there was a discrepancy between the two methods, GA as determined by the clinical examination was selected; 2) of appropriate size for GA; 3) receiving only tube feedings; 4) have no congenital anomalies affecting oral feeding (heart or oral structures); and 5) be free of chronic medical complications including severe bronchopulmonary dysplasia (Walsh et al., 2006), intraventricular hemorrhages III or IV (Papile et al., 1978), periventricular leukomalacia (de Vries et al., 1992), or necrotizing enterocolitis (Bell et al., 1978).

5.3.2 Interventions

The uni-O stimulation consisted of stroking the cheeks, lips, tongue and gums for 12 minutes and non-nutritive sucking for 3 minutes, twice a day, total 30 minutes/day (Fucile et al., 2002). This particular uni-O stimulation was selected because we previously demonstrated that it enhances nutritive sucking skills (Fucile et al., 2005). The uni-T/K stimulation involved stroking of the head, neck, trunk, and limbs for 10 minutes as well as passive range of motion of the limbs for 5 minutes, twice a day, total 30 minutes/day (Field et al., 1986). This particular uni-T/K stimulation protocol was selected because it has been found to improve infants' oral feeding performance (Rausch, 1981; White & Labarba, 1976). The multi-O+T/K stimulation consisted of oral and tactile/kinesthetic input similar to the above, each for 15 minutes, once a day in random order, total 30 minutes/day (Field et al., 1986). The control intervention consisted of the researcher (SF) placing her hands in the isolette without touching the infant for 15 minutes, twice a day, total 30 minutes/day. This particular control was designed to eliminate any possible effects of the daily presence of the researcher at the bedside. No human touch was provided during the intervention to this group because static touch i.e.

placing of hands on the infants' head and abdomen has been shown to have physiological benefits, specifically a decrease in oxygen requirement and to promote a more organized behavioral state in preterm infants 27-32 weeks gestation (Jay, 1982). Therefore, such benefits might have influenced nutritive sucking skills.

5.3.3 Outcomes

The following nutritive sucking skills were monitored: *stage of sucking* was assessed using a 5-point scale defined by Lau et al. (2000); *sucking burst duration* was defined as time of active sucking delineated by periods of pauses ≥ 1.5 seconds (sec); *sucking rate* was described as number of suction and/or expression components per second (suction &/or expression/sec); and *suction and expression amplitudes* (mmHg).

These parameters were selected based on the evidence that a more advanced stage of sucking, longer sucking burst duration, faster sucking rate, and greater suction and expression amplitudes reflect more highly developed (mature) nutritive sucking skills (Hack et al., 1985; Lau et al., 2000; Medoff-Cooper, Bilker, & Kaplan, 2001; Medoff-Cooper, Verklan, & Carlson, 1993; Sameroff, 1968; Wolff, 1968).

5.3.4 Instrumentation

A nipple bottle apparatus was used to measure these nutritive sucking skills (Lau et al., 1997). This system used nipples that were available in the nursery. The apparatus allowed for the simultaneous recording of suction and expression components. The suction component was monitored from a Mikro-tip sensor transducer (model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a catheter flush with the tip of the nipple. The expression component was monitored via another Mikro-tip sensor (model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a silastic

compressible tube to 0.5 cm from the tip of the nipple. To ensure the proper recording of the expression component, the silastic tube was positioned upward against the hard palate. The transducers were connected to a Biopac MP 1000 WSP System (Biopac Systems, Inc., Santa Barbara, CA) linked to a laptop computer. Suction and expression components were monitored on a computer screen providing direct feedback to the researcher during the course of the study. Data were stored for later analyses using the Acknowledge software program version 3.9.1 included with the Biopac system. Refer to Lau et al. (1997) for more details on the nipple bottle apparatus.

5.3.5 Procedures

A randomized trial was carried out. After parental written consent was obtained, infants were randomized into uni-O, uni-T/K, multi-O + T/K, or control group using a stratified blocked randomization with a block size of eight. Stratification by GA (26-29 vs. 30-32 weeks GA) was used to ensure that the four groups had similar GA distribution, and also stratification by time (per 3 months) to make certain that each group had similar distribution of attending neonatologists. All participants were followed from the start of the study until hospital discharge.

All four interventions were commenced 48 hours following discontinuation of nasal continuous positive airway pressure. The interventions were offered for 10 days, within a 14-day period. They were administered 15 to 30 minutes prior to the morning and afternoon tube feeding. All interventions were provided when infants were clinically stable as determined by nurse's or attending physician's recommendations and chart review, and when infants were in an optimal behavior state i.e. drowsy, quiet or active awake (Als, 1996). Interventions were halted if infants demonstrated any of the following

signs of distress: apnea, bradycardia, oxygen desaturation, fussing (denoted by flailing arms and legs), crying, or emesis. All interventions were administered in the isolette by the same researcher (SF). A screen was placed around the infants' bedside in order to 'blind' family members and caretakers to group assignment.

Nutritive sucking skills were monitored for three oral feeding sessions, when infants were taking 1-2, 3-5, and 6-8 oral feedings/day. To make sure results were not biased, the following potential covariates were taken into consideration: severity of illness using the Nursery Neurobiologic Risk Score which provides an overall score (Brazy et al., 1991), number of infants receiving all or partial breast feeding and co-interventions (occupational, physical and/or speech therapy), and number of parental visits. As well, postmenstrual age, days of life, weight, behavioral state of the infant at each 5 minute interval of the oral feeding session using a 3-point scale (1=asleep, 2=drowsy/awake, 3=fussy/crying), and episodes of apnea, bradycardia and/or oxygen desaturation at the 3 monitored oral feeding sessions were noted.

Each participant was assigned a random number to ensure blinding of the assessor for the nutritive sucking skills analyses. The introduction and advancement of oral feeding was left to the sole discretion of the attending neonatologist. Nurses were responsible for feeding the infants in their customary manner. Both the attending neonatologists and nurses were blind to group allocation. No encouragement, such as chin or cheek support, was provided during the monitored oral feeding sessions. For this study, only yellow standard nipples were utilized during the monitored oral feeding sessions (Similac Infant Nipple, Ross Laboratories, Columbus, OH, USA). The orogastric

tube, if present, was removed prior to the start of the feeding sessions. The duration of the oral feeding sessions was no longer than 20 minutes, as per nursery protocol.

5.3.6 Statistical analyses

A weighted average was used for the analyses of all outcomes of nutritive sucking skills. The weighted average was calculated from 3 sucking bursts occurring at the first, second and final third of the oral feeding session, and was computed using the following formula: $(T1*B1 + T2*B2 + T3*B3) / (T1 + T2 + T3)$, whereby T1, T2, T3 correspond to the duration (sec) of the respective sucking bursts, and B1, B2, B3 relate to the average value of a particular sucking burst measure. Sucking bursts were delineated by periods of pauses ≥ 1.5 seconds. The 3 sucking bursts analyzed were selected on the basis that their duration and stage of sucking were representative of the sucking stages and duration of sucking bursts within each period of the entire feeding session.

To assess the effect of uni-O, uni-T/K, and multi-O+T/K stimulations on nutritive sucking outcomes repeated measures ANOVA was used to compare between and within group differences over time. In case of statistical significance, post-hoc Bonferonni tests were used to assess differences between groups and time. For the purpose of this study, post-hoc group and time effects were analyzed, but post-hoc group by time interaction effects were not analyzed because the clinical significance is marginal and further analyses would not add more to our understanding of the underlying mechanism of each intervention. Significance was set at 0.05. Analyses were performed using the Statistical Program for Social Sciences software version 15.0 (SPSS, Inc, Chicago, IL). Sample size was adequate to detect differences at the $p=0.05$ level, with a power of 0.80 (Fucile et al., 2008).

5.4 Results

5.4.1 Participants

Baseline characteristics of the 75 preterm infants are summarized in Table 1. Infants in all 4 groups were comparable for GA, birth weight, gender distribution, Apgar score at 5 minutes, severity of illness, number of breast feeding and co-interventions, and number of parental visits. Ethnicity was not equally distributed between the 4 groups. However, the ethnic distribution is reflective of Harris County, Houston, TX the location where the study was conducted. The covariates during the monitored oral feeding session, including postmenstrual age, weight, behavior state and occurrence of apnea/bradycardia /oxygen desaturation were equally distributed between the four groups (Table 2).

5.4.2 Nutritive sucking skills

The stage of sucking analyses (Figure 1) indicated a significant group effect ($F_{3,27}=5.222$, $p=0.007$), time effect ($F_{2,20}=12.059$, $p<0.001$), and group x time interaction ($F_{5,49}=2.930$, $p=0.022$). Post-hoc Bonferroni tests indicated that only the uni-O group achieved a significantly more advanced stage of sucking compared to the control group ($p=0.003$). There were no differences between the 3 experimental groups (all tests $p\geq 0.350$). Over time, stage of sucking at 1-2 oral feedings/day differed significantly from 6-8 oral feedings/day ($p<0.001$).

Table 3 illustrates that there was no significant difference between the four groups with respect to sucking burst duration ($F_{3,25}=1.716$, $p=0.195$) and sucking rate ($F_{3,30}=1.859$, $p=0.159$). Over time, only sucking rate increased significantly from 1-2 to 3-5 and from 3-5 to 6-8 oral feedings/day (all tests $p\leq 0.046$).

In suction amplitude (Figure 2) there was a significant group effect ($F_{3,26}=4.804$, $p=0.011$), but no time effect ($F_{2,15}=3.272$, $p=0.076$), and no group x time interaction ($F_{5,58}=0.633$, $p=0.674$). Post-hoc Bonferroni tests indicated that suction amplitude was greater in the uni-O compared to the control and multi-O+T/K groups (all tests $p\leq 0.035$). No other group comparisons were significant (all tests $p\geq 0.540$).

In expression amplitude (Figure 3), there was a significant group effect ($F_{3,15}=8.347$, $p=0.006$), time effect ($F_{2,14}=8.434$, $p=0.007$), and group x time interaction ($F_{5,58}=11.360$, $p=0.001$). Post-hoc Bonferroni tests indicated that the uni-O group had significantly greater expression amplitudes than the control and uni-T/K groups (all tests $p\leq 0.026$). All other group comparisons were not significant (all tests $p\geq 0.370$). Over time, expression amplitude at 1-2 and 3-5 oral feedings/day differed significantly from 6-8 oral feedings/day (all tests $p\leq 0.040$).

5.5 Discussion

The aims of this study were to assess the effect of three pre-feeding sensorimotor interventions on the nutritive sucking skills of preterm infants and to investigate the impact of uni- versus multi-sensorimotor interventions on preterm infants' nutritive sucking skills. The multi-O+T/K did not lead to more advanced nutritive sucking skills than the uni-sensorimotor stimulations. Rather, the uni-O group had better nutritive sucking skills than the control, uni-T/K and multi-O+T/K groups. In earlier work, we demonstrated that 15 minutes of uni-O stimulation resulted in greater amplitude of the expression component of sucking. We now found that 30 minutes of uni-O stimulation allowed for more rapid maturation of the stages of sucking and greater amplitude of the suction as well as expression components of sucking.

5.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions

Results indicate that the uni-O stimulation was the only intervention that resulted in more advanced nutritive sucking skills, specifically stage of sucking, and suction and expression amplitudes compared to the control group. The uni-O and control groups had similar baseline characteristics and severity of illness. This eliminates the possibility that the uni-O group had better nutritive sucking skills because they were more mature or healthier than the control group.

The uni-O stimulation involved stroking of the cheeks, lips, gums and tongue as well as non-nutritive sucking on a pacifier. This may have increased the strength, endurance, and synchronization of the oral musculature leading to more advanced stages of sucking and greater suction and expression amplitudes. These enhanced nutritive sucking skills likely contributed to infants' improved oral feeding performance (proficiency, volume transfer, and rate of transfer) observed in our earlier work (Fucile et al., 2008), because stages of sucking and suction amplitude were shown to be positively correlated with volume transfer and rate of transfer (Lau et al., 2000; Sameroff, 1968).

The uni-O stimulation, however, did not lead to longer sucking burst durations or sucking rates. Nutritive sucking is generally accepted to be under the control of a central pattern generator, located in the brainstem reticular formation, where intra-oral afferent input is used to adapt the sucking pattern to changing environmental stimuli (Barlow & Estep, 2006; Finan & Barlow, 1998). Our results suggest that infants adapt their nutritive sucking pattern by exerting greater suction and expression amplitudes rather than using the other sucking skills, such as sucking burst duration and sucking rate to maximize oral feeding performance. The concept that infants are able to adapt their nutritive sucking

pattern to attain optimal feeding performance under varying circumstances is supported by the work of Sameroff (1968), Mathew (1991), and Scheel et al. (2005). These studies demonstrated that infants can self-regulate their sucking skills to attain maximal oral feeding performance, specifically rate of transfer. But the mechanism of how some nutritive sucking skills are chosen over others remains to be elucidated.

The 30 minutes of uni-O stimulation, in this study improved stages of sucking as well as the generation of suction and expression amplitudes. In our earlier work 15 minutes of the same uni-O stimulation increased only the generation of expression amplitude (Fucile et al., 2005). The generation of expression and suction entail similar peri-oral muscles, including the temporal, masseter, orbicularis oris, and suprahyoid muscles as well as jaw motions which are biphasic (Tamura et al., 1996). However, the activities of the muscles involved in the generation of suction are more complex than those used for expression. Suction is generated by maintaining a tight lip seal, lowering the jaw, elevating the lateral portions and lowering the medial portion of the tongue to provide for milk passage. Expression occurs from raising the jaw and elevation of the medial portion of the tongue to compress the nipple against the hard palate (Eishima, 1991; Tamura et al., 1996). It is conceivable that the intervention to achieve better suction must be longer than for expression because it is a more complex behavior. Hence, the duration of the sensorimotor input would be an important determinant for the achievement of specific nutritive sucking skills.

The uni-T/K and multi-O+T/K stimulation did not lead to better nutritive sucking skills compared to the control group. The uni-T/K provided sensorimotor input to the head, neck, trunk and limbs which are structures that support sucking (Bosma, 1973;

Comrie & Helm, 1997; Eishima, 1991; Redstone & West, 2004). The oral musculature was not directly stimulated which may account for the lack of difference in nutritive sucking skills between uni-T/K and controls. The multi-O+T/K also did not significantly improve preterm infants' nutritive sucking skills. This was an unexpected finding as we found earlier that 15 minutes of uni-O improved the expression component (Fucile et al., 2005). Nutritive sucking is one of many other factors involved in the achievement of safe and successful oral feeding. It is plausible that infants in both groups utilized other functions, such as more coordinated suck-swallow-respiration rather than nutritive sucking to achieve improved oral feeding performance observed in our earlier work (Fucile et al., 2008). Further studies are needed to clarify which components are selected over others to achieve an optimal oral feeding performance.

5.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions

The multi-O+T/K did not lead to an additive or synergistic effect compared to either of the uni-sensorimotor interventions. Notably, the uni-O stimulation led to more advanced nutritive sucking skills, specifically greater suction and expression amplitudes than either multi-O+T/K or uni-T/K, respectively. This suggests that the improved nutritive sucking skills noted with the uni-O stimulation are due to both the direct stimulation and longer duration of the sensorimotor input to the oral structures. If this assumption is correct, then the sensorimotor input must specifically target the end organ, i.e. the oral musculature, to achieve its specific effect.

5.5.3 Development of nutritive sucking skills

We anticipated that all nutritive sucking skills monitored would improve throughout the oral feeding sessions as infants matured. However, only stages of sucking,

suction amplitude, and sucking rate increased over time. There was no significant difference over time in expression amplitude and sucking burst duration. Given that nutritive sucking skills are under the control of a central pattern generator, as previously stated (Barlow & Estep, 2006; Finan & Barlow, 1998), it is postulated that the lack of consistent increase in all nutritive sucking skills may be due to infants' ability to adapt their nutritive sucking skills to attain the safest and most efficient oral feeding performance as shown in several other studies (Mathew, 1991; Sameroff, 1968; Scheel et al., 2005). Furthermore, ability to coordinate suck-swallow-respiration is a critical factor in achieving safe and successful oral feeding (Goldfield et al., 2006). Hence, the lack of improvement of some of the nutritive sucking skill components over time may be influenced by infants' ability to coordinate their suck-swallow-respiration processes.

5.6 Conclusion

This study demonstrated that only uni-O stimulation improved specific components of nutritive sucking skills in preterm infants. This finding emphasizes that development of nutritive sucking skills is influenced by early training experiences to the oral structures directly involved in the generation of sucking as well as neurological maturation. Moreover, the findings suggest that the duration of the sensorimotor input is also an important determinant of specific nutritive sucking skills. Precise sensorimotor interventions now exist to improve specific nutritive sucking skills permitting more efficient clinical management of oral feeding.

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5.8 References

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5.9 Tables and figures

Table 1: Participant characteristics

	Uni-oral (n=19)	Uni-tactile/ kinesthetic (n=18)	Multi- (O+T/K) (n=18)	Control (n=20)	<i>P</i> [†]
Gestational age (wks)	29.6 (1.5)	29.1 (2.0)	29.0 (1.8)	29.4 (1.9)	0.689
Birth weight (g)	1359.7 (341.1)	1325.4 (324.7)	1329.6 (293.0)	1346.6 (358.3)	0.988
Gender distribution (male/female)	12/7	11/7	10/8	16/4	0.057 [‡]
Apgar score (5 min)	8.1 (0.4)	8.5 (0.5)	8.3 (0.7)	8.3 (0.5)	0.089
Ethnic Distribution					
African American	8	3	4	5	0.010 [‡]
Caucasian	6	4	9	3	
Hispanic	5	11	5	12	
Severity of illness (NBRS)	2.6 (1.4)	2.4 (1.6)	2.3 (1.4)	2.5 (1.7)	0.916
No. infants had breastfeeding	4	8	5	6	0.241 [‡]
No. infants had co- interventions	10	15	13	14	0.117 [‡]
No. parental visits	18.6 (11.3)	21.8 (13.4)	21.6 (10.8)	24.3 (14.2)	0.577

NBRS- Nursery Neurobiologic Risk Score, No.-number, Data presented as means (SD) or number of infants, [†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

Table 2: Covariates

	Uni-oral (n=19)	Uni-tactile/ kinesthetic (n=18)	Multi- (O+T/K) (n=18)	Control (n=20)	<i>P</i> [†]
<hr/>					
1-2 PO/day					
PMA (wks)	34.4 (1.5)	34.4 (1.7)	34.0 (1.1)	34.2 (1.5)	0.716
Weight (g)	2058.7 (355.7)	2179.6 (440.9)	2069.9 (228.5)	2013.9 (277.1)	0.485
Behavior state	2	2	2	2	0.409
No. infants a/b/o ₂	1	3	0	4	0.155 [‡]
<hr/>					
3-5 PO/day					
PMA (wks)	35.4 (1.6)	36.6 (6.4)	35.4 (5.1)	35.9 (1.8)	0.823
Weight (g)	2246.5 (288.5)	2367.2 (463.4)	2213.6 (239.4)	2250.6 (289.3)	0.529
Behavior state	2	2	2	2	0.985
No. infants a/b/o ₂	2	1	2	3	0.629 [‡]
<hr/>					
6-8 PO/day					
PMA (wks)	37.1 (3.9)	35.9 (1.9)	36.2 (4.3)	36.6 (2.1)	0.681
Weight (g)	2403.4 (278.9)	2527.8 (436.8)	2335.6 (297.0)	2481.9 (376.0)	0.372
Behavior state	2	2	2	2	0.510
No. infants a/b/o ₂	0	2	0	2	0.247 [‡]

PO-oral feedings/day, PMA-postmenstrual age, No-number, a/b/o₂ . apnea/bradycardia/oxygen desaturation episodes, Data presented as means (SD) or number of infants, [†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

Table 3: Nutritive sucking outcomes at the three monitored oral feeding sessions

	Uni-oral (n=19)	Uni-tactile/ kinesthetic (n=18)	Multi- (O+T/K) (n=18)	Control (n=20)	Marginal means over time
Sucking burst duration (sec)					
1-2 PO/day	12.9 (4.6)	15.5 (6.9)	17.0 (8.7)	11.7 (5.1)	14.3 (6.3)
3-5 PO/day	10.2 (2.7)	15.8 (4.1)	16.9 (10.1)	12.2 (4.8)	13.8 (5.4)
6-8 PO/day	11.7 (3.6)	15.0 (3.8)	14.8 (6.4)	14.3 (6.6)	14.0 (5.1)
Marginal means between groups	11.6 (3.6)	15.4 (4.9)	16.2 (8.4)	12.7 (5.5)	
Suck rate (S &/or E per sec)					
1-2 PO/day ^{*,**}	0.9 (0.2)	0.9 (0.2)	0.9 (0.1)	0.8 (0.2)	0.9 (0.2)
3-5 PO/day ^{**}	1.0 (0.1)	1.0 (0.2)	0.9 (0.1)	0.8 (0.1)	0.9 (0.1)
6-8 PO/day	1.0 (0.2)	1.0 (0.2)	1.0 (0.2)	1.0 (0.2)	1.0 (0.2)
Marginal means between groups	1.0 (0.2)	1.0 (0.2)	0.9 (0.1)	0.9 (0.2)	

PO-oral feedings/day, S-suction, E-expression, Data presented as means (SD)

Repeated measures ANOVA followed by Bonferroni test ^{*} p < 0.05 vs. 3-5 oral feedings/day,

^{**} p < 0.05 vs. 6-8 oral feedings/day

Figure 1: Stages of sucking at the three monitored oral feeding sessions.

Data presented as means and SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated that only the uni-O stimulation group had significantly more advanced stages of sucking than the control group ($p=0.003$). There was a significant increase in stage of sucking over time from 1-2 to 6-8 oral feedings/day ($p<0.001$).

Figure 1

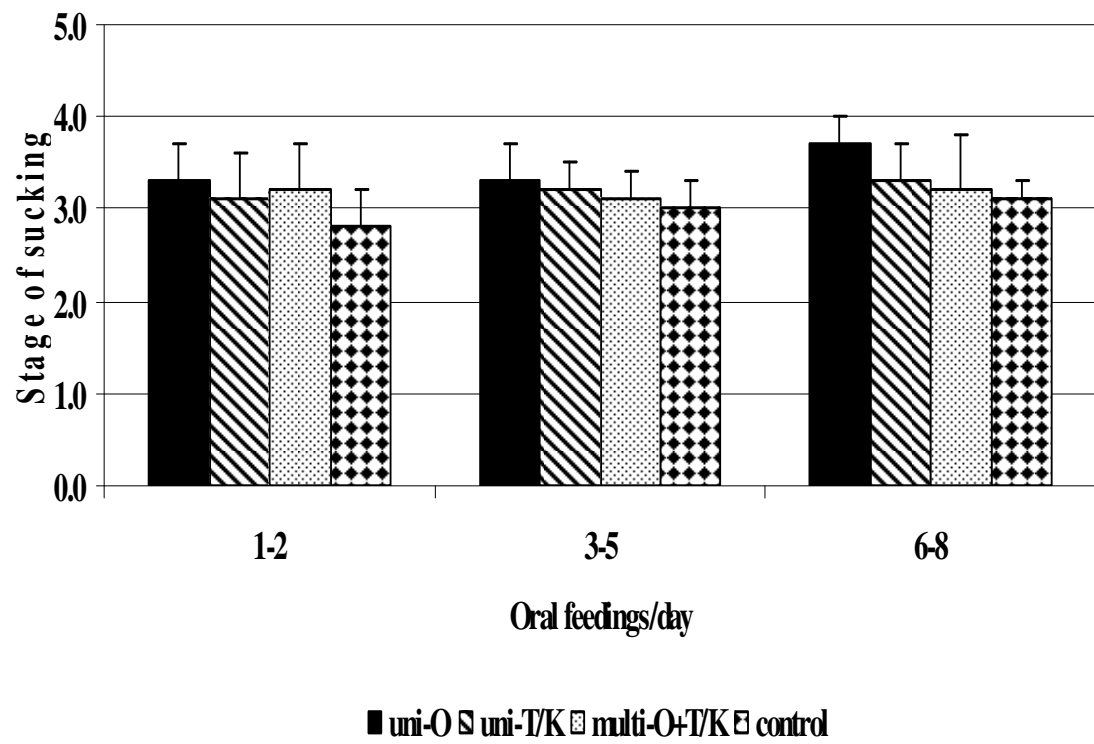


Figure 2: Suction amplitude at the three monitored oral feeding sessions.

Data presented as means and SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in suction amplitude between uni-O and control, as well as multi-O+T/K groups (all tests $p \leq 0.035$). There was no significant difference in suction amplitude over time ($p=0.076$).

Figure 2

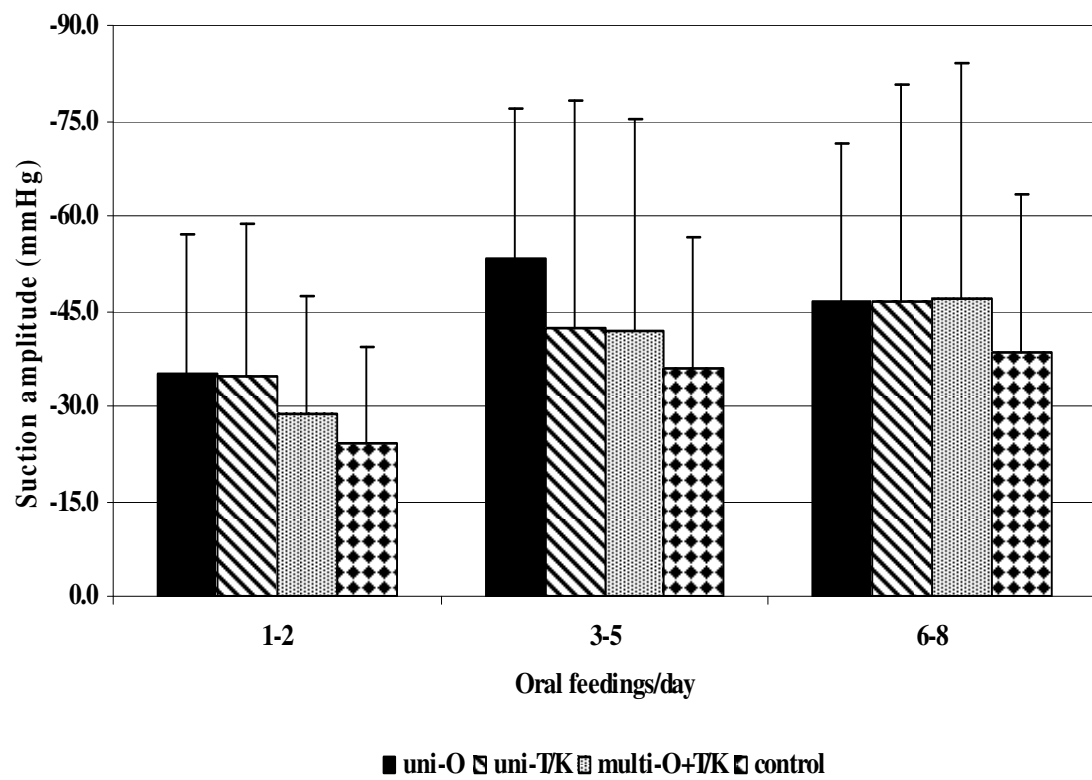
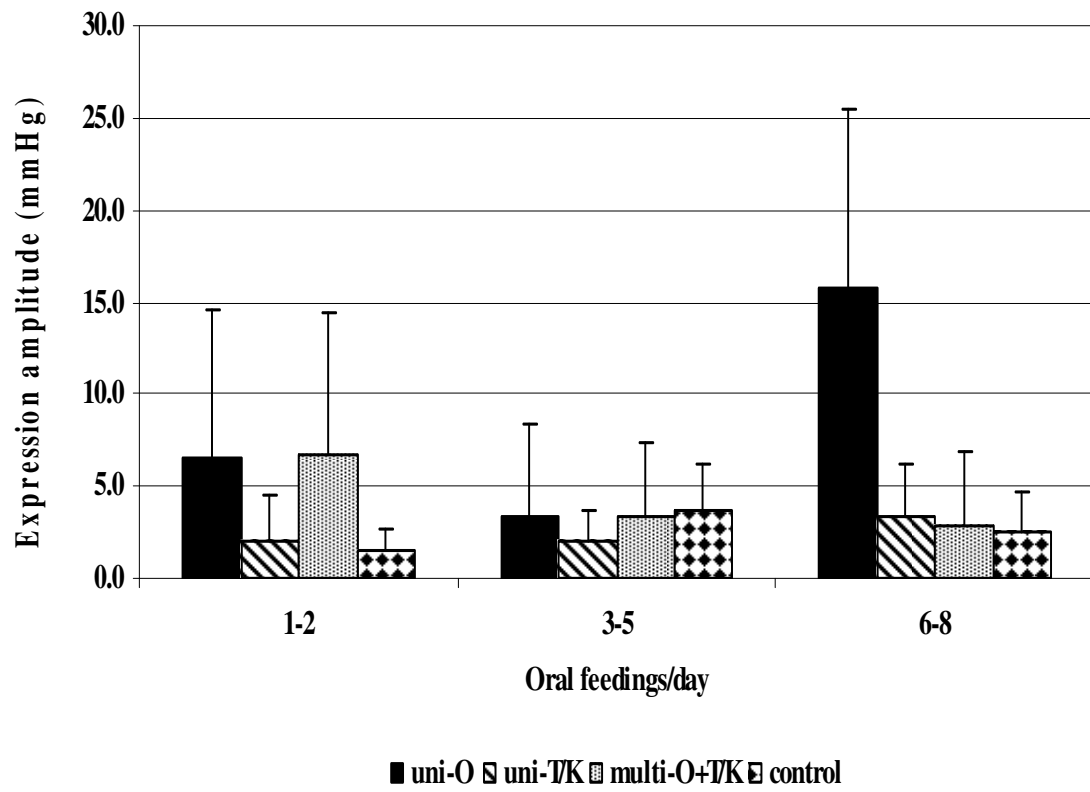


Figure 3: Expression amplitude at the three monitored oral feeding sessions.

Data presented as means and SD. Repeated measures ANOVA followed by post-hoc Bonferroni tests indicated a significant group difference in expression amplitude between uni-O and control, as well as uni-T/K groups (all tests $p \leq 0.026$), and a significant increase in expression amplitude from 1-2 to 6-8 and 3-5 to 6-8 oral feedings/day (all tests $p \leq 0.040$).

Figure 3



CHAPTER 6

INTRODUCTION TO MANUSCRIPT 3

“IMPROVEMENT OF PRETERM INFANTS’ SUCK-SWALLOW-RESPIRATION COORDINATION WITH PRE-FEEDING SENSORIMOTOR INTERVENTIONS”

In the first manuscript we found that uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations enhanced oral feeding performance of preterm infants to the same degree (Fucile et al., 2008a). Our second manuscript showed that the improved oral feeding performance in infants who received the uni-oral stimulation was due to more advanced nutritive sucking skills (Fucile et al., 2008b). However, the uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations did not enhance preterm infants’ nutritive sucking skills (Fucile et al., 2008b). Other underlying mechanisms appear to be mediating the beneficial effects associated with uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic stimulations. One key aspect involved in oral feeding is the requisite coordination of sucking and swallowing with breathing (Bu'Lock et al., 1990; Goldfield et al., 2006). Although our understanding is far from complete, we are beginning to understand the normal developmental time course as well as the physiological mechanisms underlying normal suck-swallow-respiration during non-nutritive and nutritive swallowing. Much less is known about how early therapeutic interventions, in particular sensorimotor stimulations, may influence the improvement of suck-swallow-respiration coordination in at risk infants.

Therefore, this third manuscript was set out to assess the impact of uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations on suck-swallow-

respiration coordination, and to investigate whether simultaneous provision of multi-sensorimotor interventions (oral + tactile/kinesthetic) may have additive or synergistic effects on preterm infants suck-swallow-respiration coordination. The same group of infants as in manuscript one was examined. All infants were randomly allocated to a uni-oral, uni-tactile/kinesthetic, multi-oral + tactile/kinesthetic, or control group. Confounders potentially influencing suck-swallow-respiration coordination were examined. Suck-swallow-respiration coordination was measured as a function of the ratio of number of sucks to swallows, stability of suck-swallow interval, and occurrence of swallow-respiration patterns. All outcomes were monitored longitudinally from the start of oral feeding to independent oral feeding.

The findings from this study will reveal the effect of sensorimotor interventions on preterm infants' suck-swallow-respiration coordination, delineate the influence of uni- versus multi-sensorimotor intervention on suck-swallow-respiration coordination, and provide a better understanding of the underlying sucking, swallowing, and respiration skills that may have contributed to the observed oral feeding improvements in the three intervention groups. This information will allow us to provide more specific interventions aimed at facilitating the acquisition of suck-swallow-respiration coordination in preterm infants.

IMPROVEMENT OF PRETERM INFANTS' SUCK-SWALLOW-RESPIRATION COORDINATION WITH PRE-FEEDING SENSORIMOTOR INTERVENTIONS

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6.1 Abstract

This study aims to assess the effect of uni-oral, uni-tactile/kinesthetic, or multi-oral + tactile/kinesthetic stimulation on suck-swallow-respiration coordination in preterm infants and to establish whether multi-sensorimotor interventions lead to additive or synergistic effects in suck-swallow-respiration coordination.

A total of 75 preterm infants (26-32 weeks gestational age) were randomized into one of four groups: the uni-oral group involved sensorimotor input to the oral structures; the tactile/kinesthetic group involved sensorimotor input to the head, trunk, and limbs; the multi-oral + tactile/kinesthetic group involved oral and tactile/kinesthetic input, as above; and the control group. Outcome measures included: ratio of number of sucks to swallows, stability of suck-swallow interval (secs), and swallow-respiration patterns (%).

The ratio of number of sucks to swallows and the stability of suck-swallow intervals did not differ between the four groups (all tests $p \geq 0.181$). The three experimental groups had a more advanced swallow-respiration pattern than controls. Specifically, they had fewer swallows during prolonged respiratory pauses (pause-swallow-pause) compared to controls (all tests $p \leq 0.044$). Both the uni-T/K and multi-O+T/K groups had greater occurrence of swallows during the expiratory phase (expiration-swallow-expiration) than the control and uni-O groups (all tests $p \leq 0.039$).

All three sensorimotor interventions resulted in more advanced suck-swallow-respiration coordination. The findings support the notion that development of suck-swallow-respiration coordination is not only dependent on neuro-physiological maturation, but may be influenced by early oral and non-oral sensorimotor stimulation targeting specific systems.

6.2 Introduction

Oral feeding in the neonatal period necessitates the precise coordination between sucking, swallowing, and respiration (Bu'Lock et al., 1990; Goldfield et al., 2006).

Infants who are born prematurely frequently have difficulty coordinating suck-swallow-respiration that may put them at risk for aspiration, apnea, bradycardia and oxygen desaturation during oral feeding (Gewolb et al., 2001; Lau et al., 2003). Preterm infants commonly receive tube feedings to meet their nutritional requirements until they are able to safely coordinate sucking, swallowing and respiration without clinically significant adverse events (McCain et al., 2001).

Although, far from being completely understood, suck-swallow-respiration coordination develops gradually in the neonatal period (Gewolb & Vice, 2006b; Kelly et al., 2007; Lau et al., 2003; Mizuno & Ueda, 2003). Most investigations have looked separately at suck-swallow-respiration as a function of suck-swallow coordination (Gewolb et al., 2001; Koenig et al., 1990; Lau et al., 2003) and/or swallow-respiration coordination (Bamford et al., 1992; Gewolb & Vice, 2006b; Koenig et al., 1990; Lau et al., 2003; Mizuno & Ueda, 2003; Nixon et al., 2007). Development of suck-swallow-respiration coordination for non-nutritive and nutritive conditions differ because of the additional demands placed on the infant by the ingestion of milk with the latter, and thus, will be discussed separately.

Suck-swallow coordination is often defined using ratio of number of sucks to swallows (Gewolb et al., 2001; Hack et al., 1985; Lau et al., 2003). Coordinated non-nutritive suck-swallow coordination appears to be achieved as early as 30 weeks postmenstrual age (PMA), where the ratio of sucks to swallows increases from 4 sucks

per swallow at 1-4 days of life, to 16-30 sucks per swallow afterwards (Gryboski, 1969; Hack et al., 1985). This pattern of a high suck to swallow ratio is maintained throughout term age (Hack et al., 1985). However, in nutritive suck-swallow coordination, only a one to one suck-swallow ratio is achieved because of the constraint placed on suck and swallow by the formation of the bolus and the ingestion of milk (Gewolb et al., 2001). A coordinated 1:1 nutritive suck-swallow pattern is normally achieved by 32-34 weeks PMA (Gewolb et al., 2001).

Precise swallow-respiration coordination is vital for airway protection (Bamford et al., 1992; Gewolb & Vice, 2006b; McFarland et al., 1994). The coordination of swallowing with respiration has been assessed by identifying the respiratory phase in which swallowing occurs and further classifying the respiratory phases which precede and follow the swallow (referred to as swallow-respiration pattern). The general goals of such analyses have been to determine the overall stability of swallow-respiration coordination and its developmental time course, as well as to assess the potential airway protective and other mechanical advantages of particular swallow-respiration patterns (Gewolb & Vice, 2006b; Lau et al., 2003; McFarland et al., 1994; Mizuno & Ueda, 2003; Nixon et al., 2007). Although respiration is always inhibited to accommodate swallowing in all species, including infants and adult humans (McFarland et al., 1994; Wilson et al., 1981), certain phase relationships (i.e. swallow-respiration pattern), in particular air flow events occurring immediately before and after swallowing may be more safe and efficient than others. In this regard, it has been suggested that swallows occurring within the expiratory phase, immediately preceded and followed by expiratory flow (i.e. expiration-swallow-expiration), are potentially the safest of the swallow-

respiration patterns in developing infants (Bamford et al., 1992; Gewolb & Vice, 2006b; McFarland et al., 1994). In these cases, there is no inspiratory flow that could potentially bring residues into the open airway after the period of respiratory inhibition associated with swallowing (Gewolb & Vice, 2006b). Swallowing at the expiratory phase also has potentially important mechanical advantages, such as facilitating laryngeal elevation and cricopharyngeal sphincter opening in both adults and infants (Charbonneau et al., 2005; McFarland et al., 1994; Nixon et al., 2007). The stability of swallowing respiratory phase relationships (i.e. the same phase relationships observed across swallows) is an important indicator of the neural maturation of control mechanisms underlying swallow-respiration coordination (Bamford et al., 1992). Hence, the occurrence of swallow-respiratory patterns may be a clinical marker of the neural maturation of the suck-swallow-respiration coordinating control mechanisms.

Very little is known about the normal coordinative relationship between swallowing and breathing during non-nutritive swallowing in infants. Wilson et al., (1981) observed that swallows occur at all phases of the respiratory cycle, but with a predominance occurring during the expiratory phase in infants 31-37 weeks of gestation. However, these authors excluded swallows occurring during respiratory pauses and the study population included infants with clinical pathology, potentially biasing their results. In a recent study of 'healthy' preterm infants at term corrected age, Nixon et al. (2007) found that non-nutritive swallows during sleep and wakefulness occurred very consistently in the expiratory phase of the respiratory cycle. These findings suggest that there is some variability in swallow-respiration patterning during non-nutritive

swallowing, but by term age most infants swallow during the expiratory phase (expiration-swallow-expiration) as is the case in normal adults.

The nutritive demand to swallow adds a layer of complexity that influences the developmental time course of swallow-respiration coordination during oral feeding. Stable swallow-respiration coordination with swallows occurring consistently in the expiratory phase (expiration-swallow-expiration), during oral feeding, does not develop until past term age in infants (Gewolb & Vice, 2006b; Kelly et al., 2007; Lau et al., 2003; Miller & Kiatchoosakun, 2004). Specifically, several studies have demonstrated that during nutritive conditions, swallowing occurs in all phases of respiration in both term and preterm infants (Bamford et al., 1992; Gewolb & Vice, 2006b; Koenig et al., 1990; Lau et al., 2003; Mizuno & Ueda, 2003). However, the predominant swallow-respiration pattern in preterm infants (34-35 weeks postmenstrual age), are swallows occurring during prolonged respiratory pauses, i.e. pauses greater than those normally associated with respiratory inhibition to accommodate swallow (Gewolb & Vice, 2006b; Lau et al., 2003; Mizuno & Ueda, 2003). This type of pause has previously been referred to as 'deglutition apnea' but should not be confused with the clinically significant conditions of apnea (Guilleminault et al., 2004; Miller & Martin, 1992). As preterm infants develop, there is a decrease in the occurrence of swallows during prolonged respiratory pauses (pause-swallow-pause) and an increased occurrence of swallows during the expiratory phase (expiration-swallow-expiration; Gewolb & Vice, 2006b; Kelly et al., 2007; Mizuno & Ueda, 2003). This change in swallow-respiration pattern has been interpreted as improvement in preterm infants' ability to breathe and feed orally, at the same time

reflecting their maturing neural control mechanism (Gewolb & Vice, 2006b; Kelly et al., 2007; Mizuno & Ueda, 2003).

The acquisition of safe and efficient nutritive suck-swallow-respiration coordination in preterm infants is highly vulnerable to dysfunction because of their immaturity, neonatal morbidities, and/or environmental exposure (Burklow et al., 2002). For instance, underdevelopment of the oral musculature and respiratory system may affect infants' ability to generate an efficient suck and maintain adequate respiration throughout oral feeding (Comrie & Helm, 1997). Neonatal morbidities, such as bronchopulmonary dysplasia interfere with infants' work of breathing resulting in episodes of oxygen desaturation during oral feeding (Craig, Lee, Freer, & Laing, 1999; Gewolb & Vice, 2006a). Prolonged exposure to invasive medical intervention, such as a feeding tube, often interferes with infants' sucking ability and breathing (Shiao-Yun et al., 1995).

Preterm infants' heightened vulnerability to suck-swallow-respiration difficulties makes it imperative to develop early intervention strategies that can enhance these maturational processes (Burklow et al., 2002; Dodrill et al., 2004; Ross & Browne, 2002). In an earlier study, we found that uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations improved preterm infants' oral feeding performance (Fucile et al., 2008a). Moreover, we also found that the improved oral feeding performance in infants who received the uni-oral stimulation was due to more advanced nutritive sucking skills, but not for those who received uni-tactile/kinesthetic or multi-oral + tactile/kinesthetic stimulations (Fucile et al., 2008b). Safe and successful oral feeding not only involves nutritive sucking, but also the timely coordination of suck-

swallow-respiration, as discussed earlier (Bu'Lock et al., 1990; Goldfield et al., 2006). We propose that the improved oral feeding performance could also be due to advanced suck-swallow-respiration coordination. There is some evidence suggesting that oral and tactile/kinesthetic stimulations may enhance suck-swallow-respiration coordination through improvement of the cardio-respiratory system. Anderson & Vidyasagar (1979) suggested that non-nutritive sucking enhances vascular perfusion to the pulmonary parenchyma and alveoli, thereby facilitating gaseous exchange. Kuhn et al., (1991) found tactile/kinesthetic stimulation increased urinary levels of norepinephrine and epinephrine. These hormones mediate lung maturation and maintain cardiovascular homeostasis (Kuhn et al., 1991). Such cardio-respiratory improvements may facilitate suck-swallow-respiration coordination. Taken together, it is conceivable that oral and tactile/kinesthetic stimulation may benefit suck-swallow-respiration. Furthermore, the simultaneous provision of both stimulations may lead to additive or synergistic beneficial effects on suck-swallow-respiration coordination.

Therefore, the following hypotheses are put forth 1) preterm infants who receive an uni-oral (O), uni-tactile/kinesthetic (T/K), or multi-O+T/K stimulation will demonstrate more advanced suck-swallow-respiration coordination than infants in the control group. Specifically, they will demonstrate an equal ratio of number of sucks to swallows, a stable suck-swallow interval, and more mature swallow-respiration patterns i.e. fewer swallows during prolonged respiratory pauses (pause-swallow-pause) and more swallows during the expiratory phase (expiration-swallow-expiration) than controls; and 2) infants who receive a multi-O+T/K stimulation will demonstrate better suck-swallow-respiration coordination than infants who receive uni-O or uni-T/K stimulations singly.

The present study will provide new information on the influence of uni- as well as multi-sensorimotor interventions on suck-swallow-respiration coordination in preterm infants. A better understanding of the impact of uni- and multi-sensorimotor interventions on suck-swallow-respiration coordination is necessary in order to provide more effective and thereby more efficacious oral feeding interventions in preterm infants.

6.3 Methods

6.3.1 Participants

Seventy-five preterm infants who were born less than 32 weeks gestation, appropriate size for gestational age, and only receiving tube feedings were enrolled in the study. Infants with congenital anomalies (e.g. oral or heart defects), or those with chronic medical complications including severe bronchopulmonary dysplasia (Walsh et al., 2006), intraventricular hemorrhages III or IV (Papile et al., 1978), periventricular leukomalacia (de Vries et al., 1992), or necrotizing enterocolitis (Bell et al., 1978) were excluded from the study. Informed parental consent was obtained prior to subjects' entry into the study, following consultation with the attending physician. All participants were recruited from the neonatal intensive care unit at Texas Children's Hospital, Houston, TX, USA. The study protocol was approved by the Baylor College of Medicine Institutional Review Board for Human Research and Affiliated Hospitals.

6.3.2 Study design

A randomized trial was conducted. Upon receipt of parental written consent, each participant was randomized into a uni-O, uni-T/K, multi-O+T/K, or control group. A stratified block randomization system according to gestational age (26-29 and 30-32

weeks) was used to ensure similar distribution by age, and also stratification by time (per 3 months) to make certain each group had equal distribution of attending neonatologists.

The uni-O, uni-T/K, multi-O+T/K, and control interventions were commenced 2 days following discontinuation of nasal continuous positive airway pressure. The interventions were administered twice a day, 15 to 30 minutes prior to the morning and afternoon tube feedings, for a total 10 days, within a 2 week period. Sensorimotor interventions were provided only if infants were clinically stable determined by review of medical charts, and consulting with the attending physician or primary care nurse. The interventions were stopped if infants demonstrated any of the following signs of distress: apnea, bradycardia, oxygen desaturation, fussiness, crying, and vomiting/spitting up. During all interventions the infants remained in the isolette and a screen was placed around the bedside, so as to blind caretakers and family members. The first author (SF) was responsible for administration of all sensorimotor interventions. The hospital's infection control policies were followed for administration of the sensorimotor interventions, such as stringent hand washing and donning a clean hospital gown prior to each intervention.

All participants were followed from the start of the intervention until hospital discharge. To ensure results were not biased, the following covariates were taken into consideration: severity of illness using the Nursery Neurobiologic Risk Score which provides an overall score (Brazy et al., 1991), number of infants receiving all and/or partial breast feeding and co-interventions (occupational, physical and/or speech therapy), and number of parental visits. As well PMA, days of life, weight, behavioral state of the infant at 5 minute intervals of the oral feeding session using a 3-point scale

(1=asleep, 2= drowsy/awake, 3=fussy/crying), and episodes of apnea, bradycardia and/or oxygen desaturation at the three monitored oral feeding sessions were noted.

Suck-swallow-respiration coordination outcomes were monitored longitudinally for three oral feeding sessions, when infants were taking 1-2, 3-5, and 6-8 oral feedings/day. Monitoring of suck-swallow-respiration outcomes occurred at the infants' bedside. The duration of the oral feeding sessions was no longer than 20 minutes, per nursery protocol. The oro-gastric tube, if present, was removed prior to the start of the oral feeding sessions. Each participant was assigned a random number to ensure blinding of the analyses of suck-swallow-respiration outcomes. Nurses were responsible for feeding infants in their customary manner, but no encouragement, such as chin/cheek support, was provided during the monitored oral feeding sessions. The attending neonatologist was responsible for initiating and advancing oral feedings. Both nurses and neonatologists were blind to group assignment.

6.3.3 Interventions

The study investigated the following interventions 1) uni-O stimulation – consisted of stroking the cheeks, lips, gums, and tongue and non-nutritive sucking on a pacifier, for a total of 15 minutes, twice a day, using our previous protocol (Fucile, et al., 2002). This protocol was selected because we found that it enhances oral feeding performance and nutritive sucking skills (Fucile et al., 2005); 2) uni-T/K stimulation – involved stroking the head, neck, trunk and limbs along with passive range of motion of the limbs, for a total of 15 minutes, twice a day, based on the protocol by Field and colleagues (1986). This particular uni-T/K stimulation protocol was selected because it has been found to improve infants' oral feeding performance (Rausch, 1981; White &

Labarba, 1976); 3) multi-O+T/K stimulation – consisted of the same 15-minute oral and 15-minute tactile/kinesthetic stimulation, described above, each once per day, in random order; and 4) control intervention – involved the researcher placing her hands in the isolette but not touching the infant, for 15 minutes, twice a day. This particular control was designed to eliminate any possible effects of the daily presence of the researcher at the bedside. No human touch was provided during the control intervention because static touch, i.e. placing of hands on infants head and abdomen, has been shown to decrease oxygen requirements and lead to a more organized behavioral state in preterm infants 27-32 weeks gestation (Jay, 1982). Such benefits may influence suck-swallow-respiration coordination.

6.3.4 Outcomes

Suck-swallow-respiration coordination was monitored as a function of suck-swallow coordination and swallow-respiration phases, as commonly used in the literature (Bamford et al., 1992; Gewolb & Vice, 2006b; Gewolb et al., 2001; Lau et al., 2003; Mizuno & Ueda, 2003).

To assess suck-swallow coordination, the following outcomes were monitored: *ratio of number of sucks to swallows* determined by taking the number of expression components of suck over the number of swallows, and *stability of the suck-swallow interval* defined as the time (secs) from peak of the expression component to peak swallow using the coefficient of variation (standard deviation/mean). The expression component of sucking rather than the suction component was used in these outcomes because it is the first component to develop and it can be present with or without the suction component (Lau et al., 2000). Ratio of number of sucks to swallows and the

stability of the suck-swallow interval were monitored because there is evidence that a 1:1 suck/swallow ratio and a smaller suck-swallow interval reflect more mature suck-swallow coordination, similar to that of term infants (Bamford et al., 1992; Gewolb & Vice, 2006b; Gewolb et al., 2001).

Swallow-respiration coordination was measured as the mean percent occurrence of particular *swallow-respiration patterns* as discussed above. Similar methods have been used in other investigations exploring nutritive respiratory swallowing coordination in developing preterm and full term infants. Swallow-respiration pattern was determined using a 6 category classification system [Figure 1, Lau et al., (2003)]. These include: 1) start inspiration-swallow-end expiration (start I-Sw-end E); 2) inspiration-swallow-inspiration (I-Sw-I); 3) end inspiration-swallow-start expiration (end I-Sw-start E); 4) expiration-swallow-expiration (E-Sw-E); 5i) swallow interrupt inspiration (Sw-interrupt I); 5e) swallow interrupt expiration (Sw-interrupt E); and 6) swallow occurring during a prolonged respiratory pause of ≥ 2 seconds, previously referred to as ‘deglutition apnea.’ To avoid confusion with clinically significant apnea (Guilleminault et al., 2004; Miller & Martin, 1992), we have chosen to label this pattern swallow during prolonged respiratory pause (i.e. pause-swallow-pause, P-Sw-P) rather than ‘deglutition apnea.’ The criterion for categorizing a prolonged respiratory pause as ≥ 2 seconds is based on Bamford and colleagues’ (1992) breath-breath interval analysis during feeding epochs in term infants. These normal breath-to-breath intervals ranged between 1.2 and 2.0 seconds. Consequently, we have operationally defined a respiratory pause greater than this interval as representing a prolonged respiratory pause.

6.3.5 Instrumentation

A nipple-bottle apparatus that allows for simultaneous recording of suck, swallow, and respiration in the least invasive manner for an already medically fragile population was used in this study (Lau & Schanler, 1996).

The nipple-bottle apparatus monitored both suction and expression components of sucking. The suction component was recorded from a Mikro-tip sensor transducer (model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a catheter flush with the tip of the nipple. The expression component was monitored via another Mikro-tip sensor (model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a silastic tube to 0.5 cm from the tip of the nipple. The expression and suction components were identified when a change in pressure greater than 1 mmHg was noted. For this study, only yellow standard nipples were used during the monitored oral feedings (Similac Infant Nipple, Ross Laboratories, Columbus, OH).

Swallowing was monitored via a small drum held snugly onto the hyoid region (Lau & Schanler, 1996). Just prior to swallow, the hyoid is pulled anterior and superior which results in movement of the larynx anterior and upward to protect the airway (Derkey & Schechter, 1998; Kahrilas, 1993). The anterior and superior movement of the hyoid resulted in a pressure change inside the drum and was recorded as a biphasic wave with an initial positive or negative pressure change. We used this initial peak pressure deflection as a marker for the onset of swallow. This initial movement of the hyoid is considered to be a reliable marker for the time at which airflow is halted for the passage of the bolus (Derkey & Schechter, 1998; Lau et al., 2003). Moreover, at the beginning of each feeding session, recordings of swallows were verified by visual inspection and

marking them on the computer tracing to assure recognition of swallow patterns, in order that artifacts such as coughing, sneezing, or emesis did not lead to potentially false swallows. Such monitoring of swallows by hyoid movements, rather than pharyngeal pressure, was used as it was not deemed appropriate to introduce another invasive device in preterm infants who already have a feeding tube and possibly a nasal cannula for oxygen supplementation.

Respiratory effort was monitored via a pressure sensitive drum (15 mm in diameter) taped to the midline at the thoraco-abdominal junction (Lau & Schanler, 1996; Lau et al., 2003). This respiratory device detects changes in lung inflation as measured by chest movements (Craig et al., 1999; Tarrant, Ellis, Flack, & Selley, 1997). Inhalation (increasing thoracic circumference) caused an inward movement of the pressure drum, whereas exhalation (decreasing thoracic circumference) caused an outward movement of the pressure drum. These were recorded as a biphasic wave with a positive pressure change as a marker for inspiration and negative pressure wave as a marker for expiration. Previous investigators have demonstrated that chest wall movements correlate well with respiratory airflow events (Tarrent et al., 1997; Mizuno et al., 2003), with the additional advantage that they are completely non-invasive and do not impede the upper airway that might alter respiratory function and swallow-respiration coordination. At the beginning of each oral feeding session respiration phases were verified by visual inspection and throughout the oral feeding recording artifacts such as coughing, sneezing, or emesis were marked on the computer tracing to avoid false respiratory phase tracings.

All signals were recorded using Biopac MP 100 WSP hardware and software (Biopac Systems, Inc., Santa Barbara, CA) linked to a laptop computer and stored for later analyses.

6.3.6 Data reduction and statistical analyses

Figure 2 shows a representative tracing of a suck-swallow-respiration recording. The suck-swallow events along with the swallow-respiration pattern occurring in 3 sucking bursts occurring at the first, second and third part of the oral feeding sessions were analyzed. The 3 sucking bursts were selected on the basis that their duration and stage of sucking were representative of the entire feeding session.

The ratio of number of sucks to swallows was determined by taking the total number of expression components over the number of swallows occurring within the sucking burst. Suck-swallow intervals were determined by the time (seconds) from peak expression to peak swallow (Figure 2). The swallow-respiration pattern was determined by identifying the respiration phases that preceded and followed the swallow (Figure 2). The respiratory cycles (2 to 3) preceding the sucking bursts were used as control to determine the inspiratory and expiratory pattern.

A weighted average was used for the analyses of the sucks/swallows ratio, suck-swallow intervals, and swallow-respiration patterns. It was calculated from the 3 sucking bursts and was computed using the following formula: $(T1*B1 + T2*B2 + T3*B3) / (T1 + T2 + T3)$, where T1, T2, T3 correspond to the duration (sec) of the respective sucking bursts, and B1, B2, B3 relate to the average value of a particular sucking burst measure. Sucking bursts were delineated by periods of pauses ≥ 1.5 seconds.

Repeated measures ANOVA over time followed by post-hoc Bonferonni tests were used to compare between and within group differences on ratio of sucks/swallows, stability of suck-swallow intervals and swallow-respiration patterns. For the purpose of this study, post-hoc group and time effect were analyzed. However, post-hoc group by time interaction effect were not analyzed because the clinical significance is marginal and further analyses would not add more to our understanding of the underlying mechanism of each intervention. Significance was set at 0.05. Analyses were performed using the Statistical Program for Social Sciences software version 15.0 (SPSS, Inc, Chicago, IL). Sample size was adequate to detect differences at the $p=0.05$ level with a power of 0.80 (Fucile et al., 2008a).

6.4 Results

6.4.1 Participants

Baseline characteristics of participating preterm infants are presented in Table 1. Ethnic distribution reflects that of Harris County, Houston, TX. All covariates, specifically severity of illness, number of infants receiving breast feeding and co-interventions, number of parental visits, as well as PMA, days of life, weight, behavioral state, and episodes of apnea, bradycardia and/or oxygen desaturation at the three monitored oral feeding sessions were equally distributed between the 4 study groups (all tests $p \geq 0.066$).

6.4.2 Suck-swallow coordination

Table 2 demonstrates that there was no significant group effect, no time effect, and no group x time interaction effect for both ratio of sucks/swallows and stability of suck-swallow interval (all tests $p \geq 0.181$).

6.4.3 Swallow-respiration coordination

Table 3 illustrates the swallow-respiration pattern (mean percent) in the 4 groups at each oral feeding session. There was a significant group effect only for P-Sw-P pattern ($F_{3,30}=4.615$, $p=0.009$) and E-Sw-E pattern ($F_{3,30}=8.938$, $p=0.001$). Post-hoc Bonferroni tests indicated that all 3 experimental groups had significantly fewer P-Sw-P patterns than the control group (all tests $p\leq 0.044$) and that both the uni-T/K and multi-O+T/K group had a significantly greater occurrence of E-Sw-E pattern than either the control or uni-O groups (all tests $p\leq 0.039$). There was no time and no group x time effect for all swallow-respiration patterns (all tests $p\geq 0.342$).

6.5 Discussion

The purpose of this study was to examine the effect of uni-O, uni-T/K, and multi-O+T/K stimulations on suck-swallow-respiration coordination, and to assess the influence of uni- versus multi-sensorimotor stimulations on suck-swallow-respiration coordination. The three experimental groups had a more advanced swallow-respiration pattern. Specifically, they had fewer swallows during prolonged respiratory pauses (P-Sw-P) compared to the controls, and both the uni-T/K and multi-O+T/K group had more swallows in the expiratory phase (E-Sw-E) than the control or uni-O groups.

6.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions

Suck-swallow coordination outcomes, including ratio of number of sucks to swallows and stability of the suck-swallow interval did not differ between the four groups. Studies have shown that a stable 1:1 suck-swallow rhythm is attained as early as 32-34 weeks PMA (Gewolb & Vice, 2006b; Lau et al., 2003). The lack of difference in suck-swallow coordination may be due to the fact that infants in our study were

monitored at a mean of 34 weeks PMA (range 32-36 weeks PMA), and thus a mature suck-swallow coordination was already established.

The uni-O, uni-T/K, and multi-O+T/K stimulation reduced the occurrence of swallows during prolonged respiratory pauses (P-Sw-P) compared to the control and only the uni-T/K and multi-O+T/K groups had greater occurrence of swallows during the expiratory phase (E-Sw-E) compared to the control group. Such findings are indicative of improved swallow-respiration coordination (Gewolb & Vice, 2006b; Lau et al., 2003; Mizuno & Ueda, 2003). The improved swallow-respiration coordination in the intervention groups was not due to better baseline cardiopulmonary status, as no differences between the four groups were found in the Nursery Neurobiologic Risk Score which as part of the evaluation assesses cardiopulmonary function. Therefore, the advanced swallow-respiration coordination was the result of a system specific response to the sensorimotor input (discussed below).

We speculated that the physiological mechanisms underlying the reduced occurrence of swallows during prolonged respiratory pauses (P-Sw-P), after administration of uni-O, uni-T/K, or multi-O+T/K, would be related to improved lung function (i.e. cardio-respiratory system), as described in the introduction. Non-nutritive sucking may facilitate gaseous exchange by facilitating vascular perfusion of the lungs, and tactile/kinesthetic stimulation may mediate lung maturation and maintain cardiovascular homeostasis via increased urinary levels of norepinephrine hormones (Anderson & Vidyasagar, 1979; Kuhn et al., 1991). However, there may be other possible mechanisms that could have led to improved suck-swallow-respiration. In an earlier study we found that uni-O stimulation enhanced nutritive sucking skills (Fucile et al., 2005),

which in turn may have facilitated infants' ability to control the bolus, leading to a more coordinated swallow-respiration pattern. The uni-T/K stimulation found to increase motor activity (Field et al., 1987; Field et al., 1986) may have facilitated better postural alignment of head, neck, and trunk, allowing for a more stable base for suck-swallow-respiration (Bosma, 1973; Shaker, 1990). This last interpretation is currently under investigation.

6.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions

The multi-O+T/K stimulation when compared to the uni-O or uni-T/K stimulation did not lead to additive or synergistic benefits in suck-swallow-respiration coordination. It is likely that the multi-O+T/K did not result in additive or synergistic beneficial effects because of the shorter duration of T/K stimulation. Surprisingly, we found that both multi-O+T/K and uni-T/K stimulations led to an increase in the occurrence of the swallows during expiration (E-Sw-E) compared to the uni-O group. It is possible that both the multi-O+T/K and the uni-T/K stimulations facilitated the E-Sw-E pattern because they provided direct sensorimotor input to most of the musculoskeletal structures involved in swallowing and respiration (i.e. head, neck and trunk). In contrast, the uni-O stimulation did not facilitate an E-Sw-E respiratory pattern because it provided sensorimotor input only to some of the musculoskeletal structures involved in swallowing (i.e. tongue).

6.5.3 Suck-swallow-respiration coordination

The findings that uni-O, uni-T/K, and multi-O+T/K, improved swallow-respiration coordination compared to controls supports the notion that there is a cross-system interaction in the generation and coordination of swallow-respiration (McFarland

& Tremblay, 2006). The generation of suck-swallow-respiration involves a multitude of systems, including the musculoskeletal (oral, pharyngeal, laryngeal, and esophageal structures), cardio-respiratory, and behavioral (Burklow et al., 2002; McGrath & Braescu, 2004; Thoyre, 2003). Thus, it has numerous neuronal connections (McFarland & Tremblay, 2006). As a consequence, it may be influenced by specific, as well as divergent motor behaviors (McFarland & Tremblay, 2006), as in this study. The uni-O stimulation which targeted the oral structures and uni-T/K stimulation which targeted the trunk and limbs are distinct sensorimotor interventions that appear to have enhanced different, as well as common systems used for the production and coordination of swallow-respiration, as previously discussed. These results highlight the importance of the target of the sensorimotor input for defined outcomes, in this case suck-swallow-respiration coordination.

Contrary to other studies, we did not find an improvement in suck-swallow-respiration outcomes over time within the study groups (Gewolb & Vice, 2006b; Mizuno & Ueda, 2003). The differences may be due to the disparity in methodologies whereby these studies monitored suck-swallow-respiration coordination at specific postmenstrual ages (Gewolb & Vice, 2006b; Mizuno & Ueda, 2003), while we monitored these outcomes according to stage of oral feeding progression.

The present finding that uni-O, uni-T/K and multi-O+T/K resulted in more advanced swallow-respiration coordination compared to the control group, may in part have contributed to their improved oral feeding performances (proficiency, volume transfer and rate of transfer) observed in our earlier work (Fucile et al., 2008a). In support of this, investigators noted that coordination of swallow-respiration gradually

evolved as preterm infants' rate of transfer progressed, suggesting that improved oral feeding performance is dependent on swallow-respiration coordination (Lau et al., 2003; Mizuno & Ueda, 2003). Furthermore, Daniels et al. (1988; 1990) have shown that immature cardio-respiratory control (defined as infants who experience episodes of apnea and bradycardia during wake and/or sleep states) is related to inefficient feeding behavior, specifically slow milk intake and a small amount of milk intake in preterm infants. Hence, the more advanced swallow-respiration coordination may indeed have contributed to the improved oral feeding performance in the three experimental groups.

6.6 Conclusion

The uni-O, uni-T/K, and multi-O+T/K stimulations facilitated a more advanced swallow-respiration pattern. This finding supports the notion that the generation and coordination of suck-swallow-respiration is not only dependent on neurological maturation but may be influenced by early sensorimotor input. The findings also show that suck-swallow-respiration coordination is a highly complex process which may be improved by sensorimotor input targeting specific systems. Such knowledge makes it imperative to use sensorimotor interventions more discriminately in clinical practice that must be concordant with the specifically targeted outcomes.

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6.9 Tables and figures

Table 1: Participant baseline characteristics

	Uni-oral (n=19)	Uni-tactile/ kinesthetic (n=18)	Multi- (O+T/K) (n=18)	Control (n=20)	P^{\dagger}
GA (wks)	29.6 \pm 1.5	29.1 \pm 2.0	29.0 \pm 1.8	29.4 \pm 1.9	0.689
GA distribution					
26-29 weeks	10	8	11	9	0.266 [‡]
30-32 weeks	9	10	7	11	
Birth weight (g)	1359.7 \pm 341.1	1325.4 \pm 324.7	1329.6 \pm 293.0	1346.6 \pm 358.3	0.988
Gender distribution					
Male	12	11	10	16	0.057 [‡]
Female	7	7	8	4	
Apgar score (5 min)	8.1 \pm 0.4	8.5 \pm 0.5	8.3 \pm 0.7	8.3 \pm 0.5	0.089
Ethnic Distribution					
African American	8	3	4	5	0.010 [‡]
Caucasian	6	4	9	3	
Hispanic	5	11	5	12	

GA-gestational age, Data presented as means \pm SD or number of infants

[†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

Table 2: Suck-swallow coordination outcomes at the three monitored oral feeding sessions.

	Uni-oral	Uni-tactile/ kinesthetic	Multi- (O+T/K)	Control	Marginal means over time
Ratio of sucks/swallows					
1-2 PO/day	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.2	1.0 ± 0.2	1.1 ± 0.2
3-5 PO/day	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.2	1.0 ± 0.1	1.1 ± 0.1
6-8 PO/day	1.0 ± 0.1	1.0 ± 0.1	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2
<i>Marginal means</i>					
<i>Between groups</i>	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.2	1.0 ± 0.2	
Suck-swallow interval (sec)					
1-2 PO/day	0.3 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.3	0.4 ± 0.2
3-5 PO/day	0.4 ± 0.4	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2
6-8 PO/day	0.4 ± 0.2	0.3 ± 0.2	0.3 ± 0.3	0.2 ± 0.2	0.3 ± 0.3
<i>Marginal means</i>					
<i>Between groups</i>	0.4 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.2 ± 0.2	
PO-oral feedings/day, Data presented as means ± SD, Repeated measures ANOVA no significant group, time and group x time effect, all tests p≥0.181					

Table 3: Mean percent occurrence of swallow-respiration patterns in the study groups at the three monitored oral feeding sessions.

	Uni-oral	Uni-tactile/ kinesthetic	Multi- O+T/K	Control	Marginal means over time
Start I-Sw-End E					
1-2 PO/day	18.4 ± 11.1	11.0 ± 6.2	16.1 ± 7.9	12.1 ± 18.9	14.4 ± 11.0
3-5 PO/day	19.2 ± 10.4	12.5 ± 5.6	18.2 ± 11.9	14.4 ± 9.3	16.1 ± 9.3
6-8 PO/day	17.1 ± 6.4	13.7 ± 7.6	15.7 ± 11.4	16.2 ± 14.5	15.7 ± 10.0
Marginal means between groups	18.2 ± 9.3	12.4 ± 6.5	16.7 ± 10.4	14.2 ± 14.2	
I-Sw-I					
1-2 PO/day	21.7 ± 8.0	25.9 ± 13.4	23.2 ± 15.7	19.8 ± 10.5	22.7 ± 11.9
3-5 PO/day	21.9 ± 9.1	26.8 ± 12.3	16.9 ± 12.5	20.8 ± 10.7	21.6 ± 11.1
6-8 PO/day	19.1 ± 10.9	20.4 ± 11.1	22.2 ± 7.7	14.2 ± 9.5	19.0 ± 9.8
Marginal means between groups	20.9 ± 9.3	24.3 ± 12.3	20.8 ± 12.0	18.3 ± 10.2	
End I-Sw-Start E					
1-2 PO/day	16.0 ± 16.1	14.2 ± 8.4	13.5 ± 12.1	12.8 ± 14.5	14.1 ± 12.8
3-5 PO/day	17.2 ± 16.0	14.0 ± 9.3	14.1 ± 13.0	11.1 ± 7.3	14.1 ± 11.4
6-8 PO/day	15.2 ± 8.5	17.3 ± 7.4	13.9 ± 8.1	14.2 ± 16.1	15.1 ± 10.0
Marginal means between groups	16.1 ± 13.5	15.2 ± 8.4	13.8 ± 11.1	12.7 ± 12.6	
E-Sw-E					
1-2 PO/day	13.0 ± 8.0	20.7 ± 8.0	17.2 ± 10.3	9.1 ± 5.0	15.0 ± 7.8
3-5 PO/day	11.1 ± 8.4	20.7 ± 11.9	19.8 ± 8.3	10.2 ± 4.3	15.4 ± 8.2
6-8 PO/day	15.1 ± 7.0	18.0 ± 12.5	21.1 ± 13.6	9.0 ± 5.4	15.8 ± 9.6
Marginal means between groups	13.1 ± 7.8	19.8 ± 10.8 ^{†,‡}	19.4 ± 10.7 ^{†,‡}	9.4 ± 4.9	
Sw interrupt I					
1-2 PO/day	6.2 ± 7.3	6.1 ± 15.2	6.4 ± 11.7	5.9 ± 6.1	6.2 ± 10.1
3-5 PO/day	7.0 ± 8.2	6.3 ± 5.3	2.7 ± 3.6	2.0 ± 2.4	4.5 ± 4.9
6-8 PO/day	8.3 ± 7.6	4.3 ± 4.3	3.1 ± 3.9	6.2 ± 6.9	5.5 ± 5.7
Marginal means between groups	7.1 ± 7.7	5.6 ± 8.3	4.1 ± 6.4	4.7 ± 5.1	
Sw interrupt E					
1-2 PO/day	6.0 ± 5.4	5.6 ± 4.8	3.8 ± 3.9	3.3 ± 8.4	4.7 ± 5.6
3-5 PO/day	6.5 ± 8.0	5.6 ± 4.2	5.1 ± 5.0	9.1 ± 9.5	6.6 ± 6.7
6-8 PO/day	4.1 ± 4.6	6.1 ± 4.1	3.0 ± 6.3	6.2 ± 5.6	4.9 ± 5.2
Marginal means between groups	5.5 ± 5.3	5.8 ± 4.4	4.0 ± 5.1	6.2 ± 7.8	
P-Sw-P					
1-2 PO/day	18.7 ± 19.0	16.5 ± 11.2	17.8 ± 14.4	38.8 ± 28.6	22.9 ± 18.3
3-5 PO/day	17.2 ± 18.8	14.2 ± 9.3	23.2 ± 17.4	32.5 ± 20.7	21.8 ± 16.5
6-8 PO/day	21.1 ± 19.3	20.3 ± 22.6	21.0 ± 17.2	34.0 ± 24.7	24.1 ± 20.9
Marginal means between groups	19.0 ± 19.0 [†]	17.0 ± 14.4 [†]	20.7 ± 16.3 [†]	35.1 ± 24.6	

I-inspiration, Sw-swallow, E-expiration, PO-oral feedings/day, P-pause, Data presented as means ± SD
 Repeated measures ANOVA followed by post-hoc Bonferroni tests [†]p < 0.05 vs. control,
[‡]p < 0.05 vs. uni-oral stimulation

Figure 1: Swallow-respiration patterns. 1) start inspiration-swallow-end expiration (start I-Sw-end E); 2) inspiration-swallow-inspiration (I-Sw-I); 3) end inspiration-swallow-start expiration (end I-Sw-start E); 4) expiration-swallow-expiration (E-Sw-E); 5i) swallow interrupts inspiration (Sw-interrupt I); 5e) swallow interrupts expiration (Sw-interrupt E); and 6) pause-swallow-pause (P-Sw-P, swallows occurring at cessation of respiration ≥ 2 seconds).

Figure 1

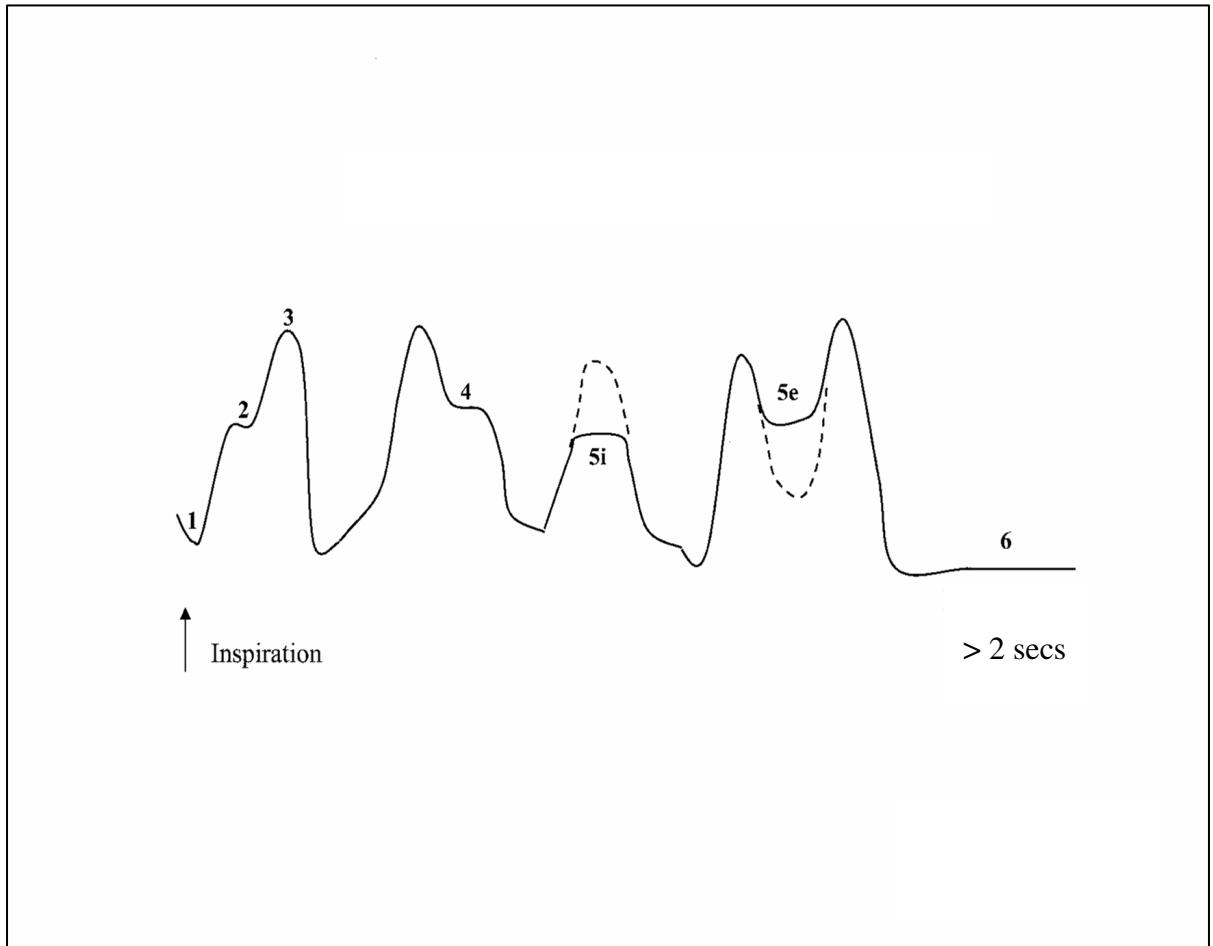
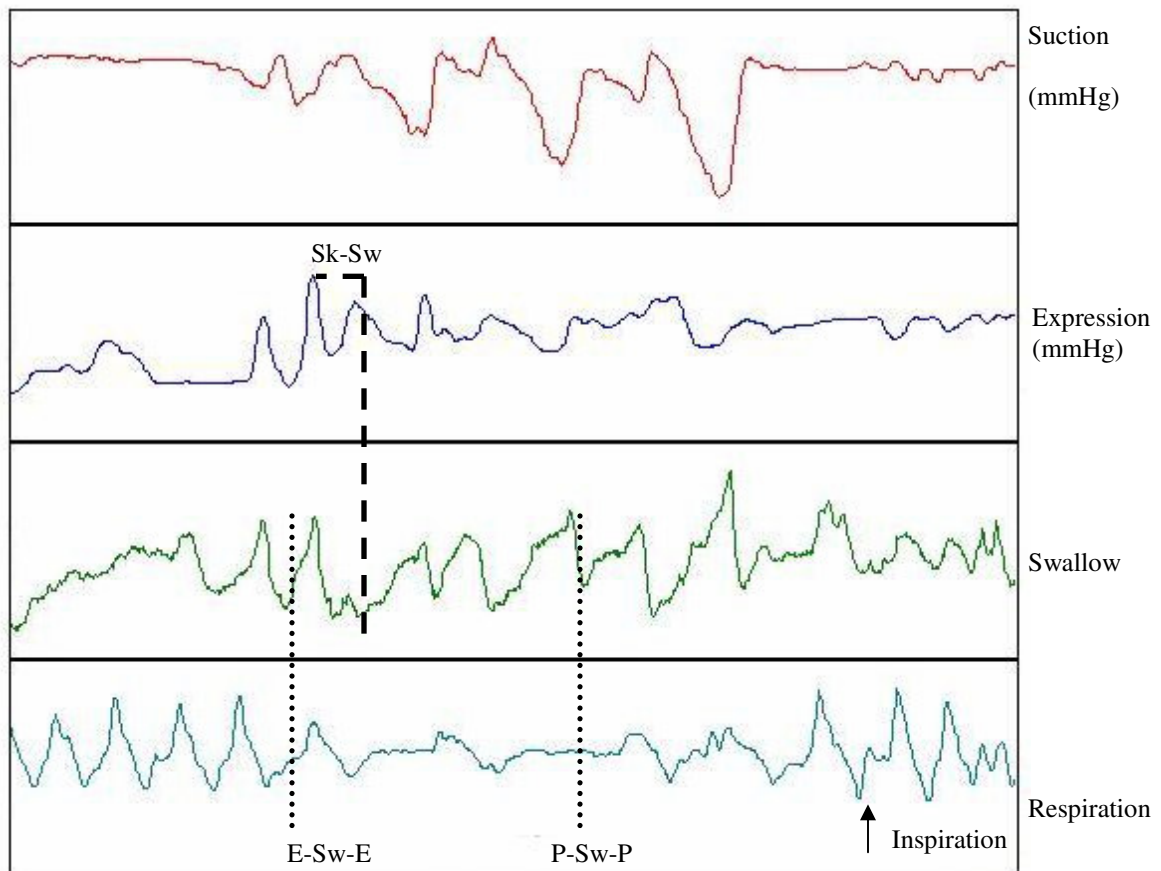


Figure 2: Sample tracing of swallow-respiration pattern, demonstrating an example of suck-swallow interval (Sk-Sw), pause-swallow-pause (P-Sw-P), and expiration-swallow-expiration pattern (E-Sw-E)

Figure 2



CHAPTER 7

INTRODUCTION TO MANUSCRIPT 4

“SENSORIMOTOR STIMULATIONS IMPROVE GROWTH AND MOTOR FUNCTION IN PRETERM INFANTS”

In the previous manuscripts we demonstrated that a pre-feeding uni-oral, uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic sensorimotor intervention enhanced preterm infants' oral feeding performance (Fucile et al., 2008a). The improved oral feeding performance in the uni-oral group was due to more advanced nutritive sucking skills and suck-swallow-respiration coordination (Fucile et al., 2008b, 2007c). However, in the uni-tactile/kinesthetic and multi-oral + tactile/kinesthetic groups it was only due to advanced suck-swallow-respiration coordination (Fucile et al., 2008c). Safe and successful oral feeding is a complex process, as pointed out before, necessitating the function and integration of multiple systems (Burklow et al., 2002; McGrath & Braescu, 2004; Thoyre, 2003). Interventions aimed at improving any one or more of the systems involved in the oral feeding process may not only ameliorate the specific system function, but may in turn also improve the oral feeding process.

There is substantial evidence demonstrating that tactile/kinesthetic stimulation affects growth (i.e. weight gain) mediated by an increase in gastrointestinal function, as well as motor activity in preterm infants (Diego et al., 2005; Dieter et al., 2003; Field, Scafidi, & Schanberg, 1987; Field et al., 1986; Mathai et al., 2001). There are inconsistent findings that oral stimulation may enhance weight gain in preterm infants (Bernbaum et al., 1983; Ernst et al., 1989; Sehgal et al., 1990). To the authors'

knowledge there is no evidence that oral stimulation affects motor function in preterm infants. We speculate that simultaneous provision of multi-sensorimotor interventions i.e. oral + tactile/kinesthetic stimulation will have an additive or synergistic beneficial effect on preterm infants' growth and motor function. Further investigations are needed to delineate the effect of a uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulation on preterm infants' growth and motor function.

This fourth manuscript, therefore, assesses the effect of these three interventions on preterm infants' growth and motor function, and explores whether multi-sensorimotor interventions lead to additive or synergistic effects on growth and motor function. The same group of infants as in manuscript one was examined. Confounders known to have an impact on growth and motor function were monitored. Growth was measured as mean daily weight gain per kilogram body weight (g/kg/day) before, during, and after the sensorimotor intervention period. Motor function was assessed using the Test of Infant Motor Performance (TIMP), a standardized neonatal motor development scale, at the end of the stimulation i.e. prior to the introduction of oral feeding.

Results from this study will more clearly establish the impact of uni-O, uni-T/K, and multi-O+T/K stimulations on preterm infants' growth and development, delineate the effect of uni- versus multi-sensorimotor interventions on growth and motor function, and provide an in-depth understanding of the underlying mechanisms mediating the improved oral feeding performance observed with the three sensorimotor interventions. Such knowledge is important in order to provide more specific interventions for a population at risk for multiple developmental disabilities.

SENSORIMOTOR STIMULATIONS IMPROVE GROWTH AND MOTOR FUNCTION IN PRETERM INFANTS

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7.1 Abstract

Background: Preterm infants are vulnerable to growth and developmental problems.

Aims: To assess the effect of uni-oral, uni-tactile/kinesthetic and multi-oral+tactile/kinesthetic stimulations on preterm infants' growth and motor function, and to determine whether provision of multi-sensorimotor interventions have an additive or synergistic effect on growth and motor function.

Study design: Seventy-five preterm infants (26-32 weeks gestation) were randomly assigned to a uni-oral group involving peri- and intra- oral stimulation; a uni-tactile/kinesthetic group consisting of body and limbs stimulation; a multi-oral+tactile/kinesthetic involving the same oral and tactile/kinesthetic stimulation as above; or a control group. Outcomes included: mean daily weight gain (g/kg/day), motor function, and length of hospital stay.

Results: The uni-oral and uni-tactile/kinesthetic group had significantly greater weight gain during the intervention period than the control group (all tests $p \leq 0.025$). The uni-tactile/kinesthetic and multi-oral+tactile/kinesthetic groups had significantly better motor function than the control group (all tests $p \leq 0.017$). There was no difference in length of hospital stay between the four groups ($p=0.792$).

Conclusions: Uni-O and uni-T/K sensorimotor interventions improved preterm infants' growth i.e. weight gain, and uni-T/K and multi-O+T/K advanced their motor function. Multi-sensorimotor stimulation did not lead to additive or synergistic beneficial effects. The findings exemplify that uni-sensorimotor interventions may lead to multiple developmental benefits, resulting in additional gains for the preterm population which is at risk for various developmental disabilities.

7.2 Introduction

Despite advances in newborn intensive care that have dramatically improved the survival of prematurely born neonates, preterm infants continue to present with poor growth and developmental delays that often extend beyond the neonatal period (Chan et al., 2001; McLeod & Sherriff, 2007; Wilson-Costello et al., 2005). Such problems decrease the health status and quality of life of children (Gilbert et al., 2003; Klassen et al., 2004). The current challenge confronting professionals in neonatal intensive care units (NICU) is not only to ensure survival, but to support and facilitate optimal growth and development in preterm infants (Als et al., 1996; Jacobs, Sokol, & Ohlsson, 2002). Hence, there is a critical need for early interventions, commencing when infants are in the NICU, aimed at enhancing infants' growth and development (Blauw-Hospers & Hadders-Algra, 2005; Gorski, 1991; Liaw, 2000).

In an earlier study we demonstrated that uni-oral, uni-tactile/kinesthetic, and multi-oral + tactile/kinesthetic stimulations ameliorated preterm infants' oral feeding performance (Fucile et al., 2008a). Oral feeding is a complex process necessitating the function and integration of multiple systems such as the musculoskeletal, cardio-respiratory, gastrointestinal, behavioral, and neurological (Burklow et al., 2002; McGrath & Braescu, 2004; Thoyre, 2003). For instance, appropriate gastrointestinal function i.e. gastric motility and emptying as well as nutrient absorption are needed for adequate acceptance of milk during oral feeding (Premji, 1998). As well, appropriate postural control is needed to maintain the physiological flexor pattern, where the hips and knees are flexed, the trunk and neck are aligned, and the hands are in midline, which provides a stable base for sucking, swallowing and respiration (Bosma, 1973; Comrie & Helm,

1997; Shaker, 1990). Hence, interventions aimed at improving any one or more of the systems involved in the oral feeding process may not only ameliorate their functions but also improve preterm infants' oral feeding performance.

There is substantial evidence demonstrating that tactile/kinesthetic stimulation increases preterm infants' gastrointestinal as well as motor function (Diego et al., 2005; Dieter et al., 2003; Field et al., 1987; Field et al., 1986; Mathai et al., 2001). Specifically, studies have found that preterm infants who received 15 minutes of tactile/kinesthetic stimulation, 3 times per day, for 5 to 10 days, demonstrated increased gastric motility and nutrient absorption leading to greater weight gain, increased motor activity (e.g. muscle tone, limb movements), and increased neurobehavioral organization (Diego et al., 2005; Dieter et al., 2003; Field et al., 1987; Field et al., 1986; Mathai et al., 2001). There are inconsistent findings that oral stimulation may enhance weight gain in preterm infants (Bernbaum et al., 1983; Ernst et al., 1989; Sehgal et al., 1990). These inconsistencies appear to be related to different methodologies used across studies (Bernbaum et al., 1983; Ernst et al., 1989; Sehgal et al., 1990). Moreover, to the authors' knowledge there is no evidence on the impact of oral stimulation on preterm infants' motor function. We postulate that oral stimulation may enhance motor function because the oral sensorimotor input may stimulate common muscles used for both oral feeding and motor functions as in control of the head, neck and/or trunk. Given that tactile/kinesthetic and oral stimulations both may enhance preterm infants' growth and motor function, we propose that simultaneous provision of multi-sensorimotor stimulations i.e. oral plus tactile/kinesthetic stimulations may have additive or synergistic beneficial effects on preterm infants' growth and motor function.

Taking the above into consideration, we hypothesize that 1) preterm infants who receive a uni-oral (O), uni-tactile/kinesthetic (T/K) or multi-O+T/K stimulation will demonstrate improved growth (i.e. weight gain) and more advanced motor functions (i.e. head and trunk control, and limb movement) than those in the control group; and 2) preterm infants who receive a multi-O+T/K stimulation will demonstrate better weight gain and motor function than those who receive uni-O or uni-T/K stimulation singly. This study will more clearly establish the effect uni-O, uni-T/K, and multi-O+T/K stimulations on preterm infants' growth and motor function, delineate the effect of uni- versus multi-sensorimotor stimulations on growth and motor function, further elucidate the underlying mechanism of the enhanced oral feeding performance observed in our earlier study, and exemplify that sensorimotor interventions have numerous developmental benefits beyond their targeted area. Such information is important in order to provide more comprehensive interventions for a population at risk for numerous developmental disorders.

7.3 Methods

7.3.1 Participants

The participants consisted of 75 preterm neonates from the NICU at Texas Children's Hospital, Houston, TX who fulfilled the following criteria: 1) gestational ages (GA) between 26-32 weeks; 2) appropriate size for their GA; 3) receiving all tube feedings; 4) absence of congenital malformations; and 5) no chronic medical illnesses, specifically severe bronchopulmonary dysplasia (Walsh et al., 2006), intraventricular hemorrhages III or IV (Papile et al., 1978), periventricular leukomalacia (de Vries et al., 1992), or necrotizing enterocolitis (Bell et al., 1978). The research protocol was reviewed

and approved by the Institutional Review Board for Human Subjects of Baylor College of Medicine and affiliated hospitals. Written parental consent was obtained prior to entry into the study.

7.3.2 Interventions

Uni-O stimulation consisted of sensorimotor input to the cheeks, lips, gums and tongue for 12 minutes and non-nutritive sucking on a pacifier for 3 minutes (Fucile et al., 2002). The infants were in supine position in the isolette throughout the uni-O stimulation. The 15-minute uni-O stimulation was administered twice per day. This uni-O stimulation was selected because it has been shown to improve oral feeding performance as well as weight gain in preterm infants (Fucile et al., 2002; Rocha et al., 2006). The uni-T/K stimulation consisted of stroking the head, neck, trunk, and limbs for 10 minutes and passive range of motion of the limbs for 5 minutes (Field et al., 1986). The infants were in the isolette, in prone and supine position respectively, during the uni-T/K stimulation. The 15-minute uni-T/K stimulation was administered twice per day. This uni-T/K stimulation was selected because it has been shown to have beneficial effects on growth and motor development in preterm infants (Field et al., 1987; Field et al., 1986). The multi-O+T/K intervention consisted of the same 15-minute uni-O and 15-minute uni-T/K stimulation as above. Each stimulation was administered once per day, in random order. The control intervention involved the researcher (SF) placing her hands in the isolette, but not touching the infant for 15 minutes, twice a day. The control intervention was designed to eliminate any possible effects of the daily presence of the researcher at the bedside.

7.3.3 Outcomes

Growth was defined as mean daily weight gain in g/kg/day. Mean daily weight gain was used as a growth outcome to standardize for gender and size differences across the groups. Mean daily weight gain was computed for three periods, before (from day of birth to first day of stimulation), during (from first to last day of stimulation) and after (from last day of stimulation to hospital discharge) the sensorimotor intervention. These time periods were selected in order to isolate and determine the direct effect of the interventions on weight gain, and whether the effect was sustained after the sensorimotor interventions.

To assess motor function, the Test of Infant Motor Performance (TIMP) was used (Campbell, 2001). The TIMP is a reliable, validated, criterion-referenced standardized assessment, measuring the postural and motor control needed for functional movement in infants from 32 weeks postmenstrual age to 4 months corrected age (Campbell, 2001; Campbell & Hedeker, 2001; Campbell, Kolobe, Osten, Lenke, & Girolami, 1995; Campbell, Kolobe, Wright, & Linacre, 2002; Campbell et al., 1999). The TIMP measures 25 elicited items and 27 spontaneous behaviors. The elicited items are administered according to standardized instructions and specifically measure orientation of the head in space, response to auditory and visual stimuli, head and trunk control, postural alignment, distal and antigravity control of limb movements. These elicited items have rating scales from 4 to 7 levels, ranging from immature to mature or minimal to full response. Spontaneous responses are scored as absent (0) or present (1). Total raw scores can range from 0-142, where higher scores represent better motor function. As well, motor behavior performance of the infants may be categorized as typical (average) and atypical (below

average or far below average) based on the raw score at different ages. Average, below, and far below average scores are within ± 1 SD, between -1 to -2 SD, and below -2.0 SD of the mean for the age group, respectively. The TIMP was administered at the end of the stimulation i.e. just prior to the introduction of oral feeding. This time point was selected in order to determine infants' motor function before the start of oral feedings.

Length of hospital stay was defined as the number of days from birth to discharge from the hospital. Length of hospital stay was monitored because sustained weight gain is a criterion for hospital discharge, and thus, if the sensorimotor interventions have beneficial effects on infants' weight gain, they would be discharged from the hospital earlier than controls (American Academy of Pediatrics, 1998).

The following variables were monitored to ensure results were not confounded by extraneous factors: severity of illness using the Nursery Neurobiologic Risk Score Assessment (Brazy et al., 1991), number of infants who received all and/or partial breast feeding sessions and co-interventions (occupational, physical and/or speech therapy), and number of parental visits throughout the study.

7.3.4 Procedures

Written consent was obtained from parents. Infants were then randomized into 1 of 4 groups: uni-O, uni-T/K, multi-O+T/K, and control. A block stratification randomization process was used based on GA (26-29 and 30-32 weeks gestation) to ensure all four groups had equal GA distribution, and also stratification by time (per 3 months) to make certain each group had equal distribution of attending neonatologists.

In addition to standard nursery care, all infants received their assigned intervention. All interventions were commenced 48 hours after discontinuation of nasal

continuous positive airway pressure and were administered in two 15-minute sessions per day (total 30 minutes per day). The two sessions were provided 15 to 30 minutes prior to a morning and afternoon feeding, with at least a three hour rest interval between the two stimulations. The interventions were administered for a total of 10 days, within a 14 day period. Interventions were not provided if infants had an increased oxygen requirement within the last 24 hours, increased occurrence of apnea/bradycardia or oxygen desaturation within the last 24 hours, and also if there was a major disruption 30 minutes prior to the start of the stimulation, such as ophthalmologic or auditory examination, based on the nurse's or attending neonatologist's recommendation and chart review. Infants' responses were closely monitored throughout the interventions. The sessions were stopped if infants presented any one of the following signs of distress: apnea, bradycardia, oxygen desaturation, fussing (denoted by splaying arms and legs), crying, and vomiting/spitting up. Prior to the intervention, a screen was placed around the bedside so as to blind nurses, neonatologists and parents. An experienced researcher (SF) was responsible for the administration of all the interventions. Infection control procedures implemented by the hospital were followed during the interventions, such as stringent hand washing and wearing a hospital gown prior to each intervention.

All participants were monitored from start of the sensorimotor intervention to hospital discharge. Nurses, who were blind to group assignment, were responsible for monitoring infants' daily weights. The TIMP was administered by the researcher (SF), who was trained in its administration.

7.3.5 Analyses

A one-way ANOVA was used to compare the effect of the four study groups on mean daily weight gain and TIMP scores. Post-hoc Bonferonni tests were used following statistical significance. A Fisher's exact test was used to compare the effect of the 4 groups on the TIMP motor behavior categories. Significance was set at 0.05. Analyses were performed using the Statistical Program for Social Sciences software version 15.0 (SPSS, Inc, Chicago, IL). Sample size was adequate to detect differences at the $p=0.05$ level with a power of 0.80 (Fucile et al., 2008a).

7.4 Results

7.4.1 Participants

All participants had similar baseline characteristics, with the exception of ethnic distribution (Table 1). The ethnic distribution reflects that of Texas Children's Hospital, Harris County, Houston, TX, where the study was conducted. All covariates were equally distributed between the four study groups (Table 2).

7.4.2 Weight gain

Table 3 illustrates a significant group difference in mean daily weight gain, only during the sensorimotor intervention period ($F_{3,71}=3.776$, $p=0.014$). Post-hoc Bonferroni tests indicated that infants in the uni-O and uni-T/K groups had significantly higher mean daily weight gains than those in the control group during the sensorimotor intervention period (all tests $p \leq 0.025$).

7.4.3 Motor function

There was a significant group difference in TIMP scores at the end of the sensorimotor intervention period ($F_{3,71}=5.213$, $p=0.015$, Table 4). Post-hoc Bonferroni

tests indicated that infants who received both uni-T/K or multi-O+T/K stimulation had significantly higher TIMP scores than those in the control group (all tests $p \leq 0.033$).

The uni-T/K and multi-O+T/K groups also had significantly greater proportions of infants who demonstrated typical (average) motor behaviors than controls (all tests $p \leq 0.017$, Figure 1).

7.4.4 Length of hospital stay

There was no difference in mean length of hospital stay between the uni-O (53.4 ± 23.3 days), uni-T/K (56.7 ± 22.3), multi-O+T/K (50.3 ± 13.9) and control groups (55.3 ± 18.9 ; $F_{3,71} = 0.346$, $p = 0.792$).

7.5 Discussion

The purpose of this study was to investigate the influence of uni-O, uni-T/K, and multi-O +T/K sensorimotor interventions on preterm infants' growth and motor function, and to delineate the effect of uni- versus multi-sensorimotor interventions on growth and motor function. The uni-O and uni-T/K during the sensorimotor intervention period resulted in significantly greater weight gain compared to controls, and both the uni-T/K and multi-O+T/K group had better motor function than controls. Although, the multi-sensorimotor intervention did not lead to additive or synergistic effects, the uni-sensorimotor intervention i.e. uni-T/K had multiple beneficial effects.

7.5.1 Uni-O, uni-T/K, and multi-O+T/K vs. control interventions

In the period before the sensorimotor intervention there was no difference in weight gain. Weight loss and limited weight gain ranges were observed across all groups, which are expected following premature birth (McLeod & Sherriff, 2007). During the sensorimotor intervention period both the uni-O and uni-T/K group gained significantly

more weight than the controls. The increase in weight gain during the sensorimotor intervention period corroborates findings from other studies (Bernbaum et al., 1983; Diego et al., 2005; Dieter et al., 2003; Field et al., 1987; Field et al., 1986; Mathai et al., 2001). Studies have shown that uni-O and uni-T/K stimulation increases gastric motility, gastric emptying, and release of hormones promoting food absorption, such as gastrin and insulin via activation of vagal tone. Such gastrointestinal improvements may have contributed to the increased weight gain observed in this study (Bernbaum et al., 1983; Ernst et al., 1989; Sehgal et al., 1990). Moreover, we observed (clinical observation) that immediately following either sensorimotor intervention, these infants were in a quiet alert and/or sleep state, expending less energy for motor activity which may have further permitted greater weight gain. The multi-O +T/K did not differ from the control group in weight gain during the sensorimotor stimulation period. The multi-O +T/K group received only 15 minutes of each stimulation which may not have been enough to have an impact on weight gain. After the sensorimotor intervention period there was no longer any difference in weight gain between all four groups. There was also no weight loss and the weight gain ranges narrowed. These findings reflect the practice of carefully monitoring caloric intake to ensure adequate weight gain in these infants. A neonatal nutritionist reviews all medical charts daily in the level 3 nursery and weekly in the level 2 nursery, and prescribes the necessary caloric amount to maintain a daily weight gain of 15-20 g/kg/day. In addition, if infants do not complete their prescribed volume of milk orally during the allotted time (20 minutes), the remaining milk is inserted into the feeding tube. However, despite such regulation of weight gain, it appears that when stimulated, infants in the uni-O and uni-T/K groups absorbed nutrients better and thus,

gained more weight than the multi-O+T/K and the control group. This increased weight gain in the uni-O and uni-T/K groups brings into focus the importance of the timing and duration of system specific sensorimotor input to achieve defined outcomes, in this case weight gain.

Infants who received the uni-T/K or multi-O+T/K stimulation had more mature motor function i.e. higher TIMP scores and more typical (average) motor behaviors than those in the control group. Note also that the proportion of infants with below average scores is larger in the controls than in the uni-T/K and multi-O+T/K groups. We further noted that the motor function of the uni-O group was not significantly different from the control group. Uni-T/K stimulation involved sensorimotor input to the head, neck, trunk and limbs and passive range of motion to the limbs. It is conceivable that the intervention facilitated the development of the musculoskeletal system specifically, head and trunk control, postural alignment, as well as limb movement (Appendix 8C). Other studies also found an increase in motor activity after administration of T/K stimulation, supporting the present findings (Field et al., 1987; Field et al., 1986; Mathai et al., 2001). The uni-O stimulation did not lead to improved motor function because it did not directly stimulate these system specific motor functions. In view of the fact that 15 minutes of uni-T/K, as part of the multi-O+T/K stimulation, resulted in improved TIMP scores suggests that that 15 minutes of uni-T/K is sufficient to have an impact on preterm infants' motor function. These results again highlight the importance of the duration of the sensorimotor input and system specific response, for defined outcomes, i.e. motor function.

The improved growth with the uni-O and uni-T/K, and better motor function with the uni-T/K and multi-O+T/K intervention may have contributed to the enhanced oral feeding performance observed in our earlier study (Fucile et al., 2008a). Infants who received 30 minutes of uni-O and uni-T/K may have benefited from improved gastrointestinal function permitting them to take larger volumes by mouth than the control group. Furthermore, tactile/kinesthetic stimulation enhanced infants' motor function in particular, head and trunk control, which likely facilitated the flexor posture needed for oral feeding, leading to improved suck-swallow-respiration coordination as demonstrated in an earlier study (Fucile et al., 2008c).

7.5.2 Multi-O+T/K vs. uni-O or uni-T/K interventions

The multi-O+T/K intervention did not lead to greater weight gain or more advanced motor function than uni-T/K intervention singly. Duration of stimulation appears to be as important as the target of the input. We have shown that 15 minutes of tactile/kinesthetic stimulation in the multi-O+T/K is sufficient to improve motor function, but if weight gain is to be achieved 30 minutes of tactile/kinesthetic stimulation is needed.

Notably, uni-sensorimotor interventions had multiple systems effects. To use the same illustration: uni-T/K improved both growth i.e. weight gain (mediated by the gastrointestinal system), as well as motor function i.e. oral-motor and postural control (mediated by the musculoskeletal system). Single, targeted sensorimotor interventions which have multiple beneficial effects are of great importance for this population who is at risk for numerous short- and long-term developmental disorders (Chan et al., 2001; McLeod & Sherriff, 2007; Wilson-Costello et al., 2005). Prospective long-term studies

are needed to establish whether the benefits of these sensorimotor interventions will persist over the long-term.

7.5.3 Length of hospital stay

There was no difference in length of hospital stay between the four groups. These findings are contrary to other studies which found a decrease in hospitalization when either uni-O or uni-T/K stimulation was provided (Field, 1986; Rocha et al., 2006). These differences may be due to discrepancies in methodologies, such as the duration of the intervention varying across all studies. Also, in our study we had no specific protocol for discharge planning, it was left to the sole discretion of the discharge planning team which certainly contributed to variation in the decision to discharge.

A limitation of this study relates to the administration of the TIMP. The researcher was not blind to group assignment. However, the TIMP is a standardized test and was administered in the same manner to all infants. Nonetheless, we suggest that the motor function outcome will need replication with ‘blind’ evaluation to confirm these results.

7.6 Conclusion

The study demonstrated that uni-sensorimotor interventions improved preterm infants’ growth and advanced their motor function. Multi-sensorimotor intervention, due to their shorter duration of each uni-sensorimotor intervention, did not lead to additive or synergistic beneficial effects. These findings show that duration of sensorimotor input is as important as the target of the sensorimotor input for defined outcomes. The findings also exemplify that uni-sensorimotor interventions may have multiple developmental benefits beyond their targeted system. With this fuller understanding of the underlying

mechanisms of sensorimotor interventions, it will be essential to use them to their greatest advantage in order to benefit a very vulnerable population of infants.

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7.9 Tables and figure

Table 1: Characteristics of preterm infants in the 4 study groups

	Uni-oral (n=19)	Uni-tactile/ kinesthetic (n=18)	Multi- O+T/K (n=18)	Control (n=20)	<i>P</i> [†]
GA (wk)					
means ± SD	29.6 ± 1.5	29.1 ± 2.0	29.0 ± 1.8	29.4 ± 1.9	0.689
(ranges)	(27-32)	(26-31)	(26-32)	(27-32)	
GA distribution (n)					
26-29/30-32 wks	10/9	8/10	11/7	9/11	0.266 [‡]
Birth weight (g)					
means ± SD	1359.7±341.1	1325.4 ± 324.7	1329.6 ± 293.0	1346.6 ± 358.3	0.988
(ranges)	(795-1956)	(900-1805)	(746-1925)	(650-2162)	
Gender distribution (n)					
Male/Female	12/7	11/7	10/8	16/4	0.057 [‡]
Apgar score (5 min)					
means ± SD wk	8.1 ± 0.4	8.5 ± 0.5	8.3 ± 0.7	8.3 ± 0.5	0.089
(ranges)	(8-9)	(8-9)	(7-9)	(7-9)	
Ethnic distribution (n)					
Afr.Ame/Cauc/Hisp	8/6/5	3/4/11	4/9/5	5/3/12	0.010 [‡]

GA-gestational age, Afr.Ame-African American, Cauc-Caucasian, Hisp-Hispanic,

[†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

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Table 2: Covariate distribution in the 4 study groups

	Uni-oral	Uni-tactile/ kinesthetic	Multi- O+T/K	Control	<i>P</i> [†]
Severity of illness (NBRS)					
means ± SD	2.6 ± 1.4	2.4 ± 1.6	2.3 ± 1.4	2.5 ± 1.7	0.916
(ranges)	(1-5)	(1-6)	(1-4)	(1-6)	
No. infants had breastfeeding	4	8	5	6	0.241 [‡]
No. infants had co-interventions	10	15	13	14	0.117 [‡]
No. parental visits					
means ± SD	18.6 ± 11.3	21.8 ± 13.4	21.6 ± 10.8	24.3 ± 14.2	0.577
(ranges)	(4-35)	(2-35)	(2-36)	(2-49)	

NBRS-nursery biologic risk score, No.- number,

[†]One-way ANOVA unless otherwise indicated, [‡]Fisher's exact test

Table 3: Mean daily weight gain before, during and after the sensorimotor interventions

	Uni-oral	Uni-tactile/ kinesthetic	Multi- O+T/K	Control	<i>P</i> [‡]
Before stimulation (g/kg/day)					
means ± SD	4.9 ± 11.1	4.0 ± 13.8	8.4 ± 7.5	5.5 ± 19.0	0.789
(ranges)	(-12 – 19)	(-45 – 16)	(-8 – 23)	(-46 – 36)	
During stimulation					
Means ± SD	17.4 ± 6.1 [*]	17.6 ± 3.8 [*]	15.7 ± 4.6	12.6 ± 5.9	0.014
(ranges)	(7 – 28)	(12 – 24)	(9 – 24)	(-4 – 22)	
After stimulation					
means ± SD	16.1 ± 6.9	15.1 ± 7.4	13.1 ± 7.3	14.3 ± 5.4	0.583
(ranges)	(1 – 30)	(4 – 36)	(2 – 32)	(5 – 24)	

^sOne-way ANOVA, ^{*}Post-hoc Bonferroni tests *p* < 0.05 vs. control

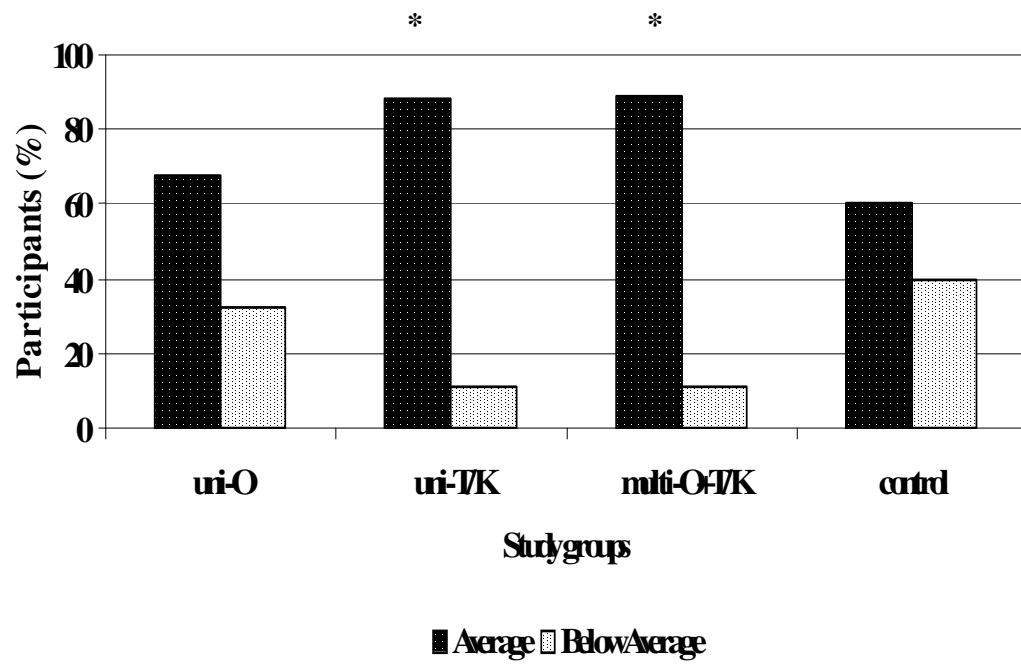
Table 4: Test of Infant Motor Performance Scores at end of the sensorimotor intervention period

	Uni-oral	Uni-tactile/ kinesthetic	Multi- O+T/K	Control	<i>P</i> [†]
TIMP Score					
means ± SD	34.6 ± 4.5	36.7 ± 4.0 [*]	36.9 ± 4.7 [*]	30.2 ± 8.2	0.003
(ranges)	(27 – 41)	(30 – 44)	(28 – 46)	(20 – 43)	

[†] 1-way ANOVA, Post-hoc Bonferroni tests ^{*} p < 0.05 vs. control

Figure 1: Test of Infant Motor Performance, percent distribution of typical and atypical motor behaviors at end of the sensorimotor intervention period. Fisher's exact test $*p < 0.017$ vs. control.

Figure 1



CHAPTER 8

DISCUSSION

The main objectives of this doctoral study were to investigate whether oral and non-oral sensorimotor stimulations, as early intervention strategies, improve oral feeding skills of preterm infants, and whether multi-sensorimotor interventions have an additive or synergistic effect leading to better oral feeding skills than uni-sensorimotor interventions. A prospective clinical trial was conducted where the impact of a pre-feeding uni-oral (O), uni-tactile/kinesthetic (T/K) and multi-O+T/K stimulation on the oral feeding skills of preterm infants was assessed, and the effect of uni-O and uni-T/K versus multi-O+T/K stimulation on oral feeding skills was compared. This chapter will highlight the main original contributions to scientific knowledge of this research, and then describe the clinical significance and implications of the research findings. Finally, the limitations of the study will be delineated and suggestions for future research will be made, followed by a conclusion.

8.1 Oral feeding performance

Independent oral feeding is an important developmental milestone that must be achieved for proper growth, development, and parent-infant bonding (Daley & Kennedy, 2000). Studies examining the effects of sensorimotor interventions on oral feeding performance in preterm infants have mainly focused on improving oral-motor function only, and assessed multi-sensorimotor interventions without distinguishing between the individual intervention effects. This study is the first to systematically address the effect of pre-feeding oral and non-oral sensorimotor stimulations on preterm infants' oral

feeding performance, and to delineate the effect of uni- versus multi-sensorimotor interventions on oral feeding performance. The following oral feeding performance outcomes were monitored: time to attainment of independent oral feeding, proficiency, volume transfer, rate of transfer and volume loss (Fucile et al., 2008a).

Results from this study provide new evidence on the beneficial effects of pre-feeding oral and non-oral sensorimotor interventions on the oral feeding performance in preterm infants (Appendix 8A). The uni-O, uni-T/K and multi-O+T/K interventions accelerated the transition from tube to independent oral feeding by 9 to 10 days, compared to the control intervention. Advancement of oral feeding, in the clinical setting, is often based on the amount of milk taken i.e. volume transfer (Premji et al., 1999). Moreover, proficiency and rate of transfer have been suggested as potential indicators of volume transfer (Lau & Schanler, 1996). Therefore, the accelerated transition to independent oral feeding could be due to improved proficiency, volume transfer, and rate of transfer observed in the 3 experimental groups. The results confirm that all three sensorimotor interventions led to greater proficiency and volume transfer, the uni-O and multi-O+T/K interventions improved rate of transfer, but only the uni-O intervention led to less volume loss (spillage) than controls (Appendix 8A). This enhanced oral feeding performance in the 3 experimental groups could not be due to a Hawthorne effect because there was no difference between the Hawthorne and control group. All 4 groups had similar baseline characteristics and health status which supports the notion that the improved oral feeding performance was the result of target specific sensorimotor input (discussed in the sections below) rather than maturation and/or better health status (Dieter & Emory, 1997).

The multi-O+T/K stimulation resulted in improved oral feeding performance compared to the control (Appendix 8A). However, it did not lead to better oral feeding performance compared to the uni-O or uni-T/K stimulations. The lack of an additive or synergistic beneficial effect may be related to the duration of the intervention. The multi-O+T/K stimulation consisted of 15 minutes rather than 30 minutes of each uni-stimulation. It is also probable that the lack of additive or synergistic effect may be due to the neuro-physiological state of the infant. In our previous study we found that 15 minutes of uni-O stimulation accelerated the transition to independent oral feeding by a mean of 8 days (Fucile et al., 2002). This oral feeding progression is similar to our current study where 30 minutes of uni-O stimulation accelerated the transition by a mean of 9 days. This finding suggests that there may be a plateau as to how fast infants may be transitioned to independent oral feeding which may be dependent on the neural integrity and controls associated with the suck-swallow-respiration cycle. In support of this, several authors have stated that sensorimotor input is effective on emerging or developing systems (Hadders-Algra, 2000; Korner, 1990). The notion that advancement to independent oral feeding is contingent on infants' neuro-physiological state necessitates further investigation.

Surprisingly, there was no difference in time to attainment of independent oral feeding, proficiency, volume transfer, rate of transfer and volume loss between the uni-O, uni-T/K, and multi-O+T/K stimulations. It is likely that there was no difference in oral feeding performance between the 3 experimental groups because these outcomes are the final common pathway for a wide range of underlying mechanisms. Analysis of more system specific mediators depicted in the oral feeding model (Appendix 8B), such as

nutritive sucking skills, suck-swallow-respiration coordination, growth (weight gain) and motor function, discussed below, will more clearly differentiate between these underlying mechanisms.

Taken together, the original finding that uni-O, uni-T/K, and multi-O+T/K improved oral feeding performance supports the notion that oral feeding is an integrated multiple systems process that may be enhanced by early training experiences which focus not only on oral but also on non-oral sensorimotor input (Dieter & Emory, 1997). Such findings highlight the importance and need for early non-oral interventions, which are currently not practiced in the clinical milieu. Greater attention needs to be paid to the influence of early non-oral stimulation because it is as an important mediator of oral feeding performance.

8.2 Nutritive sucking skills

Nutritive sucking as illustrated in the oral feeding model (Appendix 8B) is necessary for achieving safe and successful oral feeding (Lau et al., 2000; Pickler, Chiaranai, & Reyna, 2006). Nutritive sucking skills were investigated in this study in order to gain a better understanding of the underlying mechanisms that may have contributed to the observed oral feeding improvements in the three experimental groups. There is supporting evidence that oral stimulation enhances nutritive sucking skills (Fucile et al., 2002; Gaebler & Hanzlik, 1996; Leonard et al., 1980). However, the effect of tactile/kinesthetic stimulation on nutritive sucking skills, until this study, remained unknown. Moreover, the notion that multi-sensorimotor interventions may lead to better nutritive sucking skills than uni-sensorimotor intervention had not been investigated. Therefore, this study assessed and compared the effect of uni-O, uni-T/K, and multi-

O+T/K stimulations on preterm infant's nutritive sucking skills, specifically stage of sucking, sucking burst duration, sucking rate, and suction and expression amplitudes (Fucile et al., 2008b).

The uni-O stimulation was the only intervention to advance nutritive sucking skills (Appendix 8A). It led to more advanced stages of sucking, and greater suction and expression amplitudes compared to controls (Appendix 8A). Such improvements likely contributed to infants' enhanced oral feeding performance because stage of sucking and suction amplitude have been found to be positively correlated with volume transfer and rate of transfer (Lau et al., 2000; Sameroff, 1968). These findings support our previous work, whereby 15 minutes of the same uni-O stimulation increased expression amplitude (Fucile et al., 2005). However, 30 minutes of uni-O stimulation, in this study not only ameliorated expression amplitude but also improved stages of sucking and suction amplitude (Fucile et al., 2008b). These findings suggest that longer oral sensorimotor input is needed for suction because the interaction of the muscles involved in the generation of suction is more complex than that of expression (Tamura et al., 1996). Sucking burst duration and sucking rate were not increased with the uni-O stimulation. Nutritive sucking is under the control of a central pattern generator, where afferent input from the intra-oral region is used to adapt the sucking pattern to environmental stimuli (Barlow et al., 2001; Barlow & Estep, 2006; Finan & Barlow, 1998). It is likely that the lack of difference in the above nutritive sucking outcomes may be due to infants' ability to adapt their sucking pattern by exerting greater suction and expression amplitudes so that they did not need to employ these other sucking skills to maximize their oral feeding performance. Several studies support the concept that infants self-regulate their sucking

to attain optimal oral feeding performance (Mathew, 1991; Sameroff, 1968; Scheel et al., 2005).

The uni-T/K stimulation did not lead to more advanced nutritive sucking skills than controls (Appendix 8A). Neither did the multi-O+T/K stimulation compared to controls or each uni-sensorimotor intervention. Rather, 30 minutes of uni-O stimulation resulted in significantly greater suction and expression amplitudes compared to the multi-O+T/K and uni-T/K stimulations, respectively. The uni-O stimulation led to improved nutritive sucking skills over the two other interventions because it consisted of direct sensorimotor input to the oral musculature involved in the generation of sucking (Appendix 8C). The uni-T/K did not result in improvement of nutritive sucking skills because the oral musculature was not stimulated directly. The multi-O+T/K stimulation, which consisted of 15 minutes of each intervention, also did not improve preterm infants' nutritive sucking skills. This was an unexpected finding because in our previous study we showed that 15 minutes of oral stimulation improved the expression amplitude of sucking (Fucile et al., 2005). It may be that the improved oral feeding performance observed in the uni-T/K and multi-O+T/K groups is due to improvements in other underlying mechanisms associated with the oral feeding process, specifically suck-swallow-respiration coordination, weight gain and/or motor function (discussed below).

Overall, these findings confirm that development of nutritive sucking skills is not only dependent on neurological maturation, but is influenced by early training experiences of the oral musculature directly involved in the generation of sucking (Fucile et al., 2002; Lipsitt, Crook, & Booth, 1985; Sameroff, 1968). The data also bring to light the importance of system specific stimulation as well as the effect of duration of the

sensorimotor input on defined outcomes, in this case the oral muscular system for improving nutritive sucking skills (Appendix 8C). Such findings have important implications for clinical practice, because more specific oral stimulation interventions may be implemented for the development of distinct nutritive sucking skills.

8.3 Suck-swallow-respiration coordination

The oral feeding model (Appendix 8B) illustrates that safe and successful oral feeding not only entails sucking, but also proper coordination of suck-swallow-respiration processes (Bu'Lock et al., 1990; Goldfield et al., 2006). The improved oral feeding performance observed as a result of the three sensorimotor interventions could also be due to advanced suck-swallow-respiration coordination. To date, no study has investigated the effect of pre-feeding sensorimotor interventions on suck-swallow-respiration coordination in preterm infants. This study is the first to assess the effect of pre-feeding uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' suck-swallow-respiration coordination, and to examine the effect of uni- versus multi-sensorimotor interventions on suck-swallow-respiration coordination. Suck-swallow-respiration processes were monitored as a function of suck-swallow coordination, including ratio of number sucks to swallows and stability of the suck-swallow interval, and swallow-respiration coordination, specifically percent occurrence of specific swallow-respiration patterns (Fucile et al., 2008c).

The findings indicate that there was no difference in suck-swallow coordination (ratio of sucks/swallows and stability of suck-swallow interval) between the four groups (Appendix 8A). Studies have shown that mature suck-swallow coordination is established as early as 32-34 weeks PMA (Gewolb & Vice, 2006; Lau et al., 2003). Hence, there was

no difference between groups because a stable 1:1 suck-swallow rhythm was already attained when infants were first monitored at a mean of 34 weeks PMA (range 32-36 weeks PMA).

The uni-O, uni-T/K, and multi-O+T/K stimulation facilitated improved swallow-respiration coordination compared to the control group (Appendix 8A). In particular, all three sensorimotor interventions reduced the occurrence of swallows during prolonged respiratory pauses (pause-swallow-pause), and both the uni-T/K and multi-O+T/K stimulations enhanced the occurrence of swallows during the expiratory phase (expiration-swallow-expiration, Appendix 8A). Studies noted in preterm infants that with increasing age there is a decreased occurrence of swallows during prolonged respiratory pauses and an increase of swallows at the expiratory phase, which is reflective of their improved ability to breathe and feed orally at the same time (Gewolb & Vice, 2006; Kelly et al., 2007; Mizuno & Ueda, 2003). Hence, our findings are indicative of more advanced swallow-respiration coordination. This more advanced swallow-respiratory coordination may have contributed to the improved oral feeding performance observed in the three experimental groups. In support of this, investigators observed that coordination of swallow-respiration gradually evolves as preterm infants' rate of transfer progressed suggesting that improved oral feeding performance is dependent on swallow-respiration coordination (Lau et al., 2003; Mizuno & Ueda, 2003). Given that all four groups had a similar baseline cardiopulmonary status, monitored with the Nursery Neurobiologic Risk Score, eliminates the possibility that the swallow-respiration improvements could have been due to better baseline cardio-respiratory function in the intervention groups. Hence,

the improved swallow-respiration coordination resulted from the system specific response to the sensorimotor input.

It is proposed that one of the physiological mechanisms underlying the decreased occurrence of swallows during prolonged respiratory pauses (pause-swallow-pause) with all three stimulations is related to lung function (i.e. cardio-respiratory system, Appendix 8C). Anderson & Vidyasagar (1979) noted that non-nutritive sucking may facilitate gaseous exchange by enhancing vascular perfusion to the pulmonary parenchyma and alveoli, and Kuhn et al., (1991) demonstrated that tactile/kinesthetic stimulation increases urinary levels of the hormones norepinephrine and epinephrine, which mediate lung maturation and maintain cardiovascular homeostasis. Such improvements in the cardio-respiratory system, as a result of uni-O, uni-T/K, and multi-O+T/K stimulation may have contributed to the reduction in swallows during prolonged respiratory pauses (pause-swallow-pause) observed in this study.

The study results did not support the assumption that multi-sensorimotor stimulation would have an additive or synergistic beneficial effect on suck-swallow-respiration coordination (Appendix 8A). It is speculated that the multi-O+T/K did not result in additive or synergistic beneficial effects because of the shorter duration of T/K stimulation, as previously discussed. Notably, both the multi-O+T/K and uni-T/K stimulation led to improvement in the occurrence of swallows during the expiratory phase (expiration-swallow-expiration) compared to the uni-O stimulation. The multi-O+T/K and uni-T/K stimulations may have facilitated a more expiration-swallow-expiration pattern than the uni-O stimulation by providing direct sensorimotor input to most of the musculoskeletal structures involved in swallowing and respiration (i.e. head, neck and

trunk). However, the uni-O stimulation provided sensorimotor input only to some of the musculoskeletal structures involved in swallowing (i.e. tongue).

These data are the first to demonstrate that suck-swallow-respiration coordination may be enhanced by both oral and non-oral early sensorimotor interventions. These results support the concept that there may be a cross system interaction in the coordination of suck-swallow-respiration processes (McFarland & Tremblay, 2006). The generation of suck-swallow-respiration involves several systems, including the musculoskeletal (oral, pharyngeal, laryngeal, and esophageal structures), cardio-respiratory, and behavioral systems. Hence, it has numerous neuronal connections, and thereby may be influenced by divergent motor behaviors tapping into similar systems, in this case the cardio-respiratory system (McFarland & Tremblay, 2006).

Current clinical practice focuses on improving nutritive sucking skills only, and is not intended to maintain and facilitate the development of suck-swallow-respiration coordination. The beneficial effects of sensorimotor interventions on suck-swallow-respiration coordination observed in this study highlight the importance of incorporating such goals into clinical practice, to promote the acquisition of these processes in this vulnerable population.

8.4 Growth and motor function

Preterm infants are at high risk of growth and motor delays during the neonatal period which often persist into childhood (McLeod & Sherriff, 2007). Oral feeding is one of the etiological factors associated with poor growth and motor development (Gisel & Patrick, 1988; Mizuno & Ueda, 2005; Ramsay, 1995; Ramsay, Gisel, & Boutry, 1993; Reilly & Skuse, 1992). Oral feeding, as depicted in the model (Appendix 8B) necessitates

the function and integration of multiple systems (Burklow et al., 2002; McGrath & Braescu, 2004). Hence, interventions aimed at improving any one or more of the systems involved in the oral feeding process may not only ameliorate these functions but also improve preterm infants' oral feeding performance. There is substantial evidence demonstrating that tactile/kinesthetic stimulation increases preterm infants' growth i.e. weight gain, gastrointestinal function and motor function (Diego et al., 2005; Field et al.,; Field et al., 1986; Mathai et al., 2001). However, there are inconsistent findings that oral stimulation enhances growth in preterm infants (Bernbaum et al., 1983; Ernst et al., 1989; Gaebler & Hanzlik, 1996; Rocha et al., 2006; Sehgal et al., 1990). Moreover, to the authors' knowledge no study has investigated the effect of oral stimulation on motor function, nor systematically delineated the influence of uni- versus multi-sensorimotor interventions on growth and motor function. This study examined and compared the effects of uni-O, uni-T/K, and multi-O+T/K stimulation on preterm infants' growth. Specifically mean daily weight gain (g/kg/day) before, during, and after the sensorimotor intervention period. As well, motor functions were assessed using the Test of Infant Motor Performance, a standardized assessment measuring orientation of the head in space, response to auditory and visual stimuli, head and trunk control, postural alignment, distal and antigravity control of limb movements (Fucile et al., 2008d).

There was no group difference in mean daily weight gain before the sensorimotor intervention period (Appendix 8A). However, uni-O and uni-T/K stimulations resulted in better mean daily weight gain during the sensorimotor intervention period compared to controls (Appendix 8A). The multi-O+T/K stimulation did not result in better weight gain during the sensorimotor intervention compared to control and each single intervention

(Appendix 8A). The lack of a significant effect of multi-O+T/K stimulation during the sensori-motor intervention is attributed to the shorter duration of each single intervention, as discussed earlier. After the sensorimotor stimulation period there was no longer any difference between the four groups. The absence of a difference both before and after the sensorimotor intervention period between the four groups may be due to the stringent monitoring of caloric intake at Texas Children's Hospital to ensure adequate weight gain in these infants.

The finding that the uni-O and uni-T/K stimulations led to greater weight gain compared to the control group, during the stimulation period, supports previous studies (Diego et al., 2005; Field et al., 1987; Field et al., 1986; Gaebler & Hanzlik, 1996; Mathai et al., 2001; Rocha et al., 2006). It has been proposed that oral and tactile/kinesthetic stimulations increase weight gain via activation of vagal tone/activity (Dieter & Emory, 1997). Specifically, the stimulations heightened vagal tone/activity which increases intestinal motility and release of gastrointestinal hormones, such as gastrin and cholecystokinin (Diego et al., 2005; Dieter & Emory, 1997). This in turn leads to more efficient nutrient breakdown and absorption, resulting in greater weight gain (Diego et al., 2005; Dieter & Emory, 1997). Moreover, this improved gastrointestinal function may have contributed to enhanced oral feeding performance in infants who received uni-O or uni-T/K stimulation (Appendix 8C). Specifically, the improved gastrointestinal function may have permitted infants to take larger volumes by mouth than the control group (White & Labarba, 1976). Of note, the finding that despite stringent intake control infants who received uni-O and uni-T/K stimulations demonstrated increased mean daily weight gain, during the sensorimotor intervention,

highlights once more the importance of system specific sensorimotor input for defined outcomes, in this case the gastrointestinal system for weight gain.

Results indicate that infants who received the uni-T/K or multi-O+T/K stimulation, but not uni-O stimulation, had more advanced motor function i.e. higher TIMP scores and more typical (average) motor behaviors compared to those in the control group (Appendix 8A). Uni-T/K stimulation involved sensorimotor input to the head, neck, trunk and limbs and passive range of motion to the limbs. It is conceivable that the intervention facilitated the development of the musculoskeletal system specifically, head and trunk control, postural alignment, as well as limb movement (Appendix 8C). Other studies also found an increase in motor activity after administration of T/K stimulation, supporting the present findings (Field et al., 1987; Field et al., 1986; Mathai et al., 2001). The uni-O stimulation did not lead to improved motor function because it did not directly stimulate these system specific motor functions. Although, multi-O+T/K stimulation increased motor function when compared to the control group, it did not have an additive or synergistic effect on motor function because of the shorter duration of T/K stimulation (Appendix 8A). Of note, the improved motor function following the uni-T/K and multi-O+T/K stimulation may have facilitated the flexor posture during oral feeding providing a stable base for suck-swallow-respiration (Bosma, 1973; Redstone & West, 2004; Shaker, 1990). Such motor improvements may have contributed to enhanced oral feeding performance observed in these intervention groups (Appendix 8C).

Overall, these two findings above support the concept proposed earlier that duration and system specific stimulation are vital for improving defined outcomes, in this

particular case weight gain and motor function. The clinical implications are evident in that such early sensorimotor interventions ought to be implemented in practice to promote preterm infants' growth and motor development.

8.5 Length of hospital stay

Length of hospital stay is an important factor to consider in the care of preterm infants because of its effect on development, parental bonding, and financial costs to the health care system (Als, 1986, 1996; Collins et al., 2003). The criteria for discharge of preterm infants from the hospital include ability to maintain stable cardio-respiratory function, ability to maintain a normal body temperature while in an open crib, and ability to feed safely by mouth to ensure a sustained pattern of daily weight gain (American Academy of Pediatrics, 1998). Interventions aimed at improving any one of the above criteria would lead to an earlier hospital discharge. In the case of this study, it was assumed that a faster attainment of independent oral feeding and/or better weight gain would result in earlier discharge from the hospital. Although, the uni-O, uni-T/K, and multi-O+T/K groups achieved independent oral feeding sooner than the control group and the uni-O and uni-T/K had better weight gain over controls, but only during the sensorimotor stimulation period, there was no difference in length of hospital stay between the four groups. These findings are contrary to other studies which found a decrease in hospitalization when either uni-O or uni-T/K stimulation was provided (Field, 1986; Field et al., 1982; Gaebler & Hanzlik, 1996; Rocha et al., 2006). These differences may be due to discrepancies in the duration of the sensorimotor interventions across all studies (Field, 1986; Field et al., 1982; Gaebler & Hanzlik, 1996; Rocha et al., 2006). Moreover, the lack of earlier discharge in this study may be due to the fact that there was

no specific protocol for planning hospital discharge. The decision was left to the sole discretion of the discharge planning team which may have confounded the results.

8.6 Summary and synthesis of findings

The original contributions of this study to scientific knowledge are: 1) confirming that oral and non-oral sensorimotor stimulation are both effective early intervention strategies to improve the oral feeding skills of preterm infants, 2) providing evidence of the underlying systems mediating the oral feeding improvements associated with each intervention, and 3) establishing the importance of system specific sensorimotor input and duration of the input for defined outcomes. The following is a summary of new findings from this study:

- The uni-O, uni-T/K, and multi-O+T/K stimulations resulted in improved oral feeding performance compared to controls. Specifically, all three experimental groups improved time to attainment of independent oral feeding, proficiency and volume transfer. The uni-O and multi-O+T/K groups increased rate of transfer, and the uni-O group showed less volume loss (spillage) compared to controls (Appendix 8A). These results support the notion that oral feeding is a complex multiple systems process that can be enhanced by oral as well as non-oral sensorimotor interventions (Appendix 8B, C).
- The uni-O stimulation was the only sensorimotor intervention that enhanced nutritive sucking skills: stage of sucking, suction and expression amplitudes (Appendix 8A). Moreover, in an earlier study, 15 minutes of uni-O stimulation resulted in greater amplitude of the expression component of sucking (Fucile et al., 2005). However, in this study 30 minutes of uni-O stimulation allowed for

more rapid maturation of the stages of sucking and greater amplitude of the expression as well as suction component of sucking. These findings support the notion that development of nutritive sucking skills is influenced by early specific training experiences to the oral musculoskeletal system (Appendix 8C), and further demonstrate that the duration of the sensorimotor input is also an important determinant of specific nutritive sucking skills.

- The three sensorimotor interventions resulted in more advanced suck-swallow-respiration coordination than the control intervention. Specifically, all three sensorimotor interventions led to a more advanced and safer swallow-respiration pattern as manifested by fewer swallows during prolonged respiratory pauses (pause-swallow-pause) compared to the controls. Both the uni-T/K and multi-O+T/K groups had more swallows during the expiratory phase (expiration-swallow-expiration) than the control and uni-O groups (Appendix 8A). These results highlight that the generation and coordination of swallow-respiration can be influenced by early sensorimotor input, in this case targeting the cardio-respiratory system (Appendix 8C).
- The uni-O and uni-T/K stimulation resulted in significantly better growth, i.e. weight gain compared to controls, but only during the sensorimotor intervention period (Appendix 8A). The uni-T/K and multi-O+T/K groups had better motor function (Appendix 8A). These outcomes again confirm the importance of system specific stimulations in this case accessing the gastrointestinal and musculoskeletal systems for weight gain and motor function, respectively (Appendix 8C).

- The multi-sensorimotor intervention (multi-O+T/K) did not result in better oral feeding performance, nutritive sucking skills, suck-swallow-respiration coordination, growth or motor function than uni-sensorimotor interventions (i.e. uni-O or uni-T/K alone). It is proposed that the lack of an additive or synergistic effect is associated with the duration of each sensorimotor input. This result demonstrates that duration of the sensorimotor input is critical for influencing defined outcomes.
- The uni-sensorimotor interventions showed multiple systems effects, as denoted in the oral feeding model (Appendix 8C). To illustrate: uni-O stimulation resulted in improved oral feeding performance, nutritive sucking skills, suck-swallow-respiration coordination and growth, mediated by the oral musculoskeletal, cardio-respiratory, and gastrointestinal systems, respectively. The uni-T/K stimulation resulted in improved oral feeding performance, suck-swallow-respiration, growth and motor function mediated by the cardio-respiratory, gastrointestinal and whole body musculoskeletal systems, respectively. Single, targeted sensorimotor interventions which have multiple beneficial effects are of great importance for this population who is at risk for numerous short and long-term developmental disorders.

8.7 Significance and clinical implications

Advances in newborn intensive care have dramatically improved the survival of prematurely born neonates (Chan et al., 2001; Wilson-Costello et al., 2005). The current challenge confronting professionals in the neonatal intensive care unit is to optimize developmental outcomes, in particular oral feeding skills of preterm infants (Als et al.,

1996; Jacobs et al., 2002). Existing gaps in the literature needed to be addressed, specifically the effect of pre-feeding oral and non-oral sensorimotor stimulation as well as the influence of uni- versus multi-sensorimotor stimulation on preterm infants' oral feeding skills. Such information would provide a better understanding of the effects of pre-feeding sensorimotor stimulation as preventative strategies to safeguard and optimize development of preterm infants' oral feeding skills.

This study has demonstrated the benefits of early oral and non-oral sensorimotor stimulations for the enhancement of oral feeding skills in preterm infants. However, the underlying mechanisms mediating the improved oral feeding differ because each intervention taps into specific sensorimotor systems. As neonatal oral feeding difficulties may ensue from oral and non-oral origins, the present results demonstrate that the current clinical approach must expand to incorporate both oral and non-oral interventions.

This study further showed that the system specific sensorimotor input and duration of the input are important for improvement of defined outcomes. Such knowledge makes it imperative to use sensorimotor interventions more discriminately in clinical practice in order to benefit a very vulnerable population of infants.

Multi-sensorimotor stimulations, as implemented here, did not lead to additive or synergistic beneficial effects on oral feeding skills. However, the finding that uni-sensorimotor stimulation may have multiple developmental benefits beyond their targeted area is of great clinical importance for this population who is at risk for numerous short- and long-term developmental disabilities. The overall clinical implications of sensorimotor interventions are evident in that more efficacious interventions may be implemented aimed at improving more than one area of preterm infants' development.

The health care system in North America is undergoing changes shifting towards earlier hospital discharge of preterm infants in order to unite families promptly and to control costs (Collins et al., 2003). Ability to bottle/breast feed is often the remaining obstacle for hospital discharge (Collins et al., 2003). Results from this study demonstrated the effective use of a non-invasive pre-feeding oral and non-oral sensorimotor intervention as a preventative approach to enhance oral feeding skills in this high risk population. These findings emphasize the need for a critical appraisal of our current clinical practice which still focuses on remediation of oral feeding problems. A more preventative clinical approach needs to be implemented in neonatal developmental care plans because the associated benefits extend not only to the health and well being of the children and their families, but to society as a whole.

8.8 Limitations

A randomized clinical trial was conducted to reduce bias and spurious causality. However, the study has some limitations. Discharge planning was left to the sole discretion of the discharge planning team which was a likely confounder and may account for the lack of difference in length of hospitalization between groups. The implementation of a study protocol for discharge planning may have reduced such biases and possibly allowed for better discrimination between the intervention groups.

Financial constraints did not allow for the employment of a 'blind' assessor for the administration of the TIMP. Although I (the candidate), the assessor, was trained in the administration of the TIMP, I was not blind to group assignment. This may have potentially biased the results. The TIMP is a standardized test and it was administered in the same manner to all infants. Therefore, results are adequate to provide suggestive data

of the impact of sensorimotor interventions on motor performance. Replication of this part of this study with ‘blind’ evaluation is needed to confirm these results.

The effect of touch, such as holding the baby, placing hands over the head and abdomen, skin to skin contact, and breast feeding may have beneficial effects on infants’ oral feeding skills, thereby potentially biasing results (Als, 1996; Lemons & Lemons, 1996). However, all four groups received the same number of parental visits, co-interventions and breast feeding sessions which eliminates this likelihood. The control group received an intervention, designed to eliminate any possible effect of the daily presence of the researcher at the bedside. Infants in the uni-O, uni-T/K, and multi-O+T/K groups received an additional 30 minutes of touch in comparison to the control group. Given that all 3 sensorimotor stimulations ameliorated oral feeding performance to the same degree, it can be argued that “any” touch may have resulted in the positive oral feeding outcomes of this study. However, differences between groups were noted when more specific outcomes were examined such as the nutritive sucking, suck-swallow-respiration coordination, weight gain, and motor function. These discrete findings minimize the possibility that “any” touch could explain these feeding outcomes, and that “specific” touch is needed for such positive outcomes.

The sample was limited to very preterm infants, born between 26 and 32 weeks gestation. This criterion was purposely selected because a large majority of extremely preterm infants born less than 26 weeks gestation develop severe chronic medical conditions and older preterm infants greater than 32 weeks gestation generally do not present with oral feeding difficulties. Although our results may be generalized to older

and less medically vulnerable preterm infants, they cannot be extended to the younger and more medically fragile preterm infants.

Finally, this study only monitored the effect of oral and non-oral sensorimotor interventions on oral feeding skills during the hospitalization. Financial restrictions prevented long-term follow up. The long-term effects of sensorimotor interventions on infants' oral feeding skills and general development remains unknown.

8.9 Future research directions

The goal for improving survival of preterm infants has been successfully achieved by the medical profession, at the cost of increased morbidity (Chan et al., 2001; El-Metwally et al., 2000; Finnstrom et al., 1997; Stoelhorst et al., 2005; Wilson-Costello et al., 2005). Although this study has shown that early oral and non-oral sensorimotor stimulations promote the development of oral feeding skills in preterm infants more research in this area is needed to further reduce and prevent oral feeding difficulties in this highly vulnerable population.

Studies investigating which duration, intensity, and specific sensorimotor stimulation leads to the most optimal oral feeding outcomes are needed for more accurate and efficient early interventions. As well, more studies are needed which further explore the underlying mechanisms responsible for the oral feeding improvements, such as the musculoskeletal function, e.g. postural alignment during the oral feeding sessions, (Casaer et al., 1982), cardio-respiratory function, e.g. more specific analysis on the duration of swallows during prolonged respiratory pauses and/or direct monitoring of heart rate, respiratory rate, and oxygen desaturation during oral feeding, and gastrointestinal function e.g. gastrointestinal transit time. Such information would

provide a more in-depth understanding of the effects of early sensorimotor interventions and would more clearly establish the efficiency of early intervention strategies to facilitate the acquisition of competent oral feeding skills in preterm infants.

This study investigated the impact of early sensorimotor interventions in clinically stable preterm infants born between 26-29 weeks gestation. However, infants who are born less than 26 weeks gestation, as well as those with chronic medical complications, such as severe bronchopulmonary dysplasia, intraventricular hemorrhages grades III & IV, periventricular leukomalacia, and necrotizing enterocolitis are at very high risk of encountering oral feeding difficulties. It will be of great importance to determine the benefits of pre-feeding sensorimotor treatments in these infants because such an intervention may reduce and/or prevent the occurrence of oral feeding difficulties and possibly other related developmental problems.

This research assessed only the short-term effects of sensorimotor stimulation on preterm infants' oral feeding skills. Preterm infants are highly vulnerable to long-term oral feeding disorders in particular oral sensory aversions, difficulties with the transition to solid foods, growth retardation and developmental delays (Comrie & Helm, 1997; Dodrill et al., 2004; Gardner & Hagedorn, 1991). Such potential long-term consequences make it imperative to study the long-term effects of sensorimotor stimulation on oral feeding skills, in particular during the transition period from liquid to solid feeding, and on growth, developmental milestones, and independence in activities of daily living, well into childhood.

Oral feeding influences the parent-infant relationship, and the quality of life of children and their families (Burklow et al., 2002; Hawdon, Beauregard, Slattery, &

Kennedy, 2000). This study only assessed oral feeding skills of preterm infants, and did not investigate the potential positive impact it may have had on the parent-infant relationship. Investigation of parental stress, parent-infant bonding, as well as the quality of life of children and their families are warranted to gain a better understanding of the social impact of early sensorimotor interventions.

In keeping with the Developmental Care Approach parents are encouraged to become more involved in the clinical care of their child. Such sensorimotor stimulation programs can be taught to parents because they are safe, simple, and inexpensive. This will empower parents by giving them an increased opportunity to interact with their child in a positive meaningful manner early on. Hence, the effectiveness and safety of the sensorimotor interventions when administered by the parents needs to be further ascertained.

The gap between research evidence and clinical practice will continue to persist because new research knowledge is often not readily and/or easily accessible to the clinical community. More simple and diverse means of transferring research knowledge e.g. a research evidence website on neonatal oral feeding interventions, continuing education courses, or parent outreach programs, are urgently needed in order for this preventative approach to be translated and applied in routine neonatal developmental care plans.

8.10 Conclusion

Infants who are born prematurely are highly vulnerable to encounter oral feeding difficulties. This study has shown that oral feeding is a highly complex multiple systems process which is not only dependent on neurological maturation, but may be influenced by both oral and non-oral sensorimotor interventions by tapping into specific systems associated with the oral feeding process. The beneficial effects of pre-feeding oral and non-oral sensorimotor interventions on preterm infants' oral feeding skills highlight the importance of early intervention, to maintain and facilitate the acquisition of proper oral feeding skills, thereby promoting better long-term health and quality of life for infants born preterm and their families.

8.11 References

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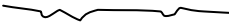
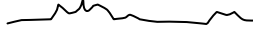




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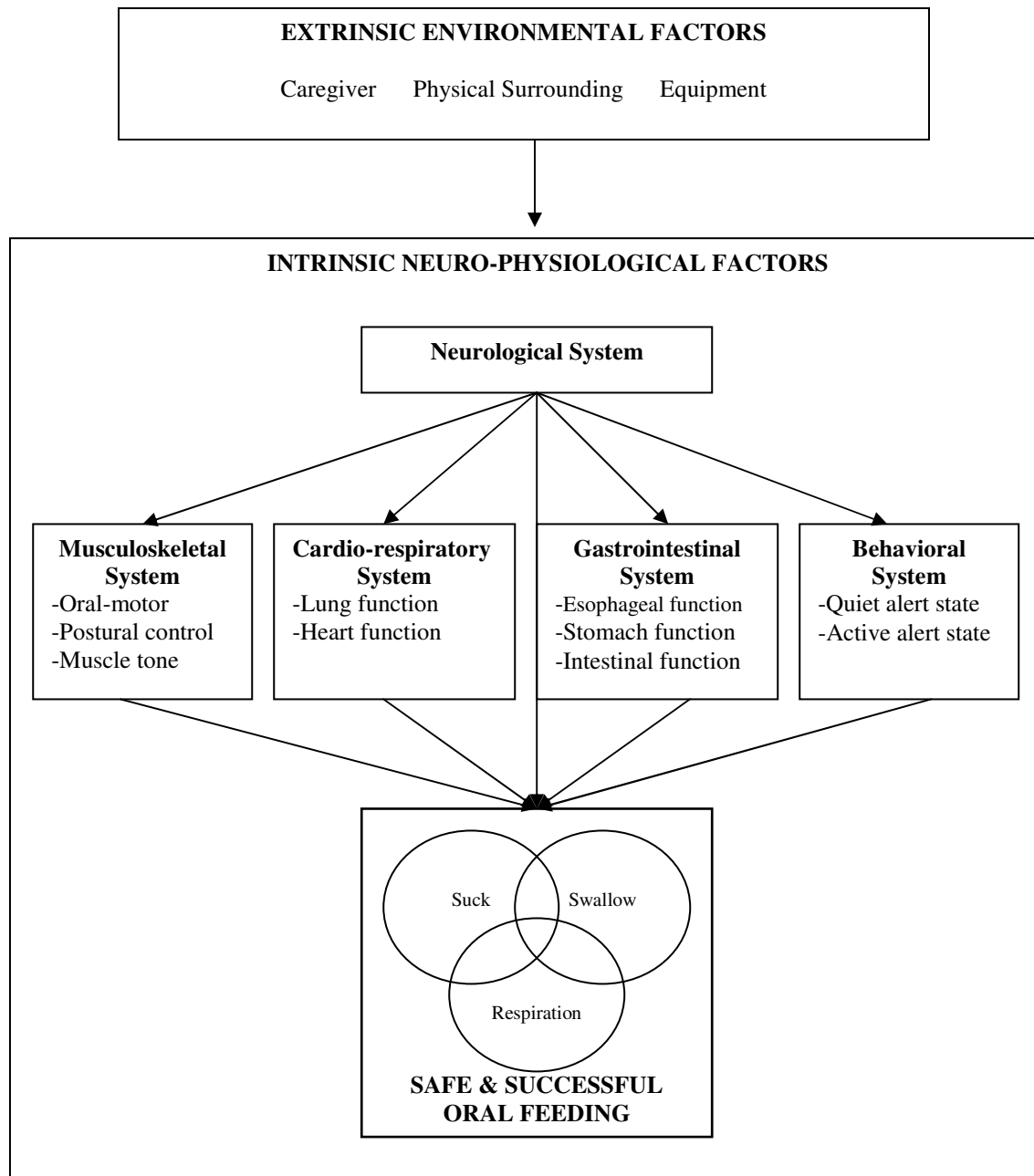
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APPENDICES

Appendix 2A: Stages of sucking scale
Lau et al. (2000), Acta Paediatr 89(7), 846-852.

Stage	Description	Sample Tracings	
1	-Arrhythmic expression with no suction. -Arrhythmic alternation of suction/expression with few sucking bursts.	Suction	
		Expression	
2	-Rhythmic expression with no suction, and/or -Arrhythmic alternation suction/expression, presence of sucking bursts.	Suction	
		Expression	
3	-Rhythmic expression with no suction, and/or -Rhythmic alternation of suction/expression: sucking burst duration is prolonged, suction amplitude overall increases, but vary over a wide range.	Suction	
		Expression	
4	-Rhythmic alternation of suction/expression: well defined suction component with less amplitude fluctuation, duration of sucking bursts prolonged. -The use of expression alone disappears.	Suction	
		Expression	
5	-Rhythmic alternation of suction/expression: well defined suction and expression, stronger suction amplitude. -Pattern similar to that observed in full term infants.	Suction	
		Expression	

Appendix 2B: Oral feeding model



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Appendix 3A: Institutional review board approval

Human Approval Letter

Page 1 of 1

March 09, 2005

CHANTAL LAU
BAYLOR COLLEGE OF MEDICINE
PEDIATRICS: NEWBORN



Baylor College of Medicine
Office of Research
Phone: (713) 798-6970
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H-16870 - SENSORY STIMULATIONS AS INTERVENTIONS FOR THE ENHANCEMENT OF ORAL FEEDING IN PRETERM INFANTS

APPROVAL VALID FROM 2/15/2005 TO 1/4/2006

Dear Dr. LAU

The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals (BCM IRB) is pleased to inform you that the research protocol and consent form(s) named above were approved.

The study may not continue after the approval period without additional IRB review and approval for continuation. You will receive an email renewal reminder notice prior to study expiration; however, it is your responsibility to assure that this study is not conducted beyond the expiration date.

Please be aware that only IRB-approved informed consent forms may be used when written informed consent is required.

Any changes in study or informed consent procedure must receive review and approval prior to implementation unless the change is necessary for the safety of subjects. In addition, you must inform the IRB of adverse events encountered during the study or of any new and significant information that may impact a research participants' safety or willingness to continue in your study.

The BCM IRB is organized and operated according to guidelines of the International Council on Harmonization, the United States Office for Human Research Protections and the United States Code of Federal Regulations and operates under Federal Wide Assurance No. 00000286, issued April 30, 2001. Affiliated hospitals include: the Veterans Affairs Medical Center, The Methodist Hospital, Texas Childrens Hospital, Texas Institute for Rehabilitation and Research, and the Harris County Hospital District.

Sincerely yours,

A handwritten signature in cursive script that reads "Mary M. Mariscalco".

MARY M MARISCALCO, M.D.
Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

<http://brain-prod.bcm.tmc.edu/esp1/reports/Human/Approval.asp?protocol=92661&title=co...> 3/10/2005

Appendix 3B: Consent form

CONSENT FORM

HIPAA Compliant

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

SENSORY STIMULATIONS AS INTERVENTIONS FOR THE ENHANCEMENT OF ORAL FEEDING IN PRETERM INFANTS

H-16870- SENSORY STIMULATIONS AS INTERVENTIONS FOR THE ENHANCEMENT OF ORAL FEEDING IN PRETERM INFANTS

Background

Infants born early frequently have difficulty feeding by mouth. As a result, their discharge from the hospital often is delayed. We do not understand well the reasons why this occurs. However, it is known that poor feeding may be due to an immature suck as well as to uncoordinated suck, swallow, and breathe. The latter may lead to poor oxygenation, choking, coughing, and aspiration of milk into the lungs.

Studies have shown that providing non-nutritive oral exercise before a baby begins to feed by mouth can improve his/her oral feeding. In addition, gentle massage to premature infants can be beneficial for their growth and development.

We have developed an oral feeding device that allows us to measure at the same time the infant's sucking, swallowing, and breathing. With this instrument, we can observe how well these 3 functions are coordinated when an infant is feeding by mouth.

This research study is sponsored by Baylor College of Medicine.

Purpose

The purpose of this research study is to evaluate how beneficial 3 interventions are in improving the oral feeding of premature infants born between 26 and 32 weeks gestation when compared to infants receiving no such interventions. The 3 interventions consist of a non-nutritive oral exercise, a gentle body massage and the combination of both.

Procedures

You will be one of approximately 84 subjects to be asked to participate in this trial. The research will be conducted at the following location(s): Baylor College of Medicine, TCH: Texas Children's Hospital.

Your baby will be assigned at random (like the toss of a coin) to one of 4 groups. All the interventions will be done once a day, for 10 days over 2 weeks. This will be started 2 days after your baby has no further need of assisted ventilation. The interventions will be conducted while your baby remains in his or her bed.

Group 1 will receive two 15-minute interventions consisting of non-nutritive exercises in and around the mouth. Group 2 will receive two 15-minute interventions consisting of a gentle body massage. Group 3 will receive two 15-minute interventions consisting of a 15-minute non-nutritive exercise intervention and a 15-minute gentle body massage. Group 4 will not receive any intervention.

Bottle feeding will be monitored when your baby is taking 1-2, 3-5, and 6-8 oral feedings per day. To measure sucking, 2 small tubes will be placed on a bottle nipple. The nipples are the ones that are commonly used in the nursery. To measure swallowing, a small drum (1/4 inch diameter) held by a soft elastic attached to a stockinette cap will be placed under your baby's chin. To measure breathing, a belt with a sensor or another drum will be placed snugly around your baby's chest. The 2 tubes from the bottle nipple, the swallowing drum, and the breathing sensor will be connected to a computer that will measure how strong your baby sucks and the rhythms of your baby's sucking, swallowing, and breathing. There will be up to 6 such recordings.

In addition to measuring how well your baby feeds by mouth, his/her motor development will also be monitored. We will videotape your baby's movement for 15 minutes after monitoring his/her feeding. Medical information will also be collected from his/her chart.

You can see and get a copy of your research related health information. Your research doctor may be able to provide you with part of your information while the study is in progress and the rest of your information at the end of the study.

CONSENT FORM
Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals
SENSORY STIMULATIONS AS INTERVENTIONS FOR THE ENHANCEMENT OF ORAL
FEEDING IN PRETERM INFANTS

HIPAA Compliant

H-16870- SENSORY STIMULATIONS AS INTERVENTIONS FOR THE ENHANCEMENT OF ORAL
FEEDING IN PRETERM INFANTS

Potential Risks and Discomforts

There is no risk in the interventions that we will provide for your baby. These procedures are not invasive. The non-nutritive oral exercise is routinely used by occupational therapists working with infants. It consists of stroking the cheeks, lips, gums, and tongue. The body massage also used by therapists, consists of gently stroking the upper and lower limbs and between the shoulders. Both interventions present minimal risk. However, the interventions and oral feeding will be stopped at the sign of any distress.

Your baby should not experience any discomfort from the small drum under the chin as it is held by a soft elastic attached to a small cap that your baby will wear.

Over the last 12 years that we have used our oral feeding monitoring instrument, we have not observed any overt interference with oral feeding in infants.

Potential Benefits

You have been told that the benefits of participating in this study may be: that your infant may be able to feed by mouth at an earlier time than currently observed. However, you may receive no benefit from participating in this study.

Alternatives

The only alternative to this study is non-participation.

Subject Costs and Payments

There are no costs to your baby's participation in this research study. You will not be paid to participate in this research study.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to be a part of the study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor may stop the study at any time.

There may be unknown risks/discomforts involved. Study staff will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study.

If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care. You will not be paid for the injury.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected

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health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

The investigator, CHANTAL LAU, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: CHANTAL LAU at 832-826-1384.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970.

Your signature on this consent form attests to the fact that your child _____ has, within limits imposed by age, maturity, and psychological state, given his/her assent (affirmative agreement) to participate in this research project.

Appendix 3C : Uni-oral stimulation

Fucile et al. (2002), J Pediatr 141(2), 230-236.

Characteristics	Stimulation Steps	Frequency	Duration
Peri-oral	Infant in supine position		
<i>Cheeks</i>	-Place index finger at base of the nose. -Move finger toward the ear, then down and towards the corner of the lip (C pattern).	4X each side	2 min
<i>Upper-lower lip</i>	-Place index finger at corner of the upper/lower lip. -Move the finger away, in a circular motion, from the corner towards the center and to the other corner.	4X each lip	2 min
<i>Upper-lower lip curl</i>	-Place index finger at center of upper/lower lip. -Apply sustained pressure, downward towards the middle.	4X each lip	2 min
<i>Jaw</i>	-Place index finger at hyoid bone. -Apply sustained pressure upward towards the chin tip.	4X	1 min
Intra-oral	Infant in supine position		
<i>Internal cheek</i>	-Place index finger at inner corner of lip. -Move back towards the molars, return to corner of lip.	4X each side	2 min
<i>Upper-lower gum</i>	-Place finger at the center of the gum, slowly move towards the back of the mouth. -Return to the center of the mouth.	4X each side	2 min
<i>Mid-blade of the tongue</i>	-Place finger at the center of the mouth. -Apply sustained pressure in the hard palate for 3 secs. -Move the finger down to the center blade of the tongue. -Displace the tongue downward with a firm pressure. -Immediately move the finger to contact the center of the mouth at the hard palate.	4X	1 min
Nonnutritive sucking	Infant in supine position		
<i>Pacifier</i>	-Place pacifier in mouth.	NA	3 min
Administration	Twice per day		
Total/day			30 min

Appendix 3D: Uni-tactile/kinesthetic stimulation

Field et al. (1986), Pediatrics 77(5), 654-658.

Characteristics	Stimulation Steps	Frequency	Duration
Tactile	Infant in prone position. Stroke with your hands		
<i>Head-Neck</i>	-From the top of the head to the neck.	12X	1 min
<i>Neck-Shoulders</i>	-From the neck across the shoulders.	12X	1 min
<i>Back</i>	-From the upper back to the waist.	12X	1 min
<i>Legs</i>	-From the thigh to the foot to the thigh on both legs.	12X	1 min
<i>Arms</i>	-From the shoulder to the hand to the shoulder on both arms.	12X	1 min
Kinesthetic	Infant in supine position. With a firm grasp starting in neutral		
<i>Right Arm</i>	-Passive flexion & extension.	6X	1 min
<i>Left Arm</i>	-Passive flexion & extension.	6X	1 min
<i>Right Leg</i>	-Passive flexion & extension.	6X	1 min
<i>Left Leg</i>	-Passive flexion & extension.	6X	1 min
<i>Both Legs</i>	-Passive flexion & extension.	6X	1 min
Tactile	Infant in prone position. Stroke with your hands		
<i>Head-Neck</i>	-From the top of the head to the neck.	12X	1 min
<i>Neck-Shoulders</i>	-From the neck across the shoulders.	12X	1 min
<i>Back</i>	-From the upper back to the waist.	12X	1 min
<i>Legs</i>	-From the thigh to the foot to the thigh on both legs.	12X	1 min
<i>Arms</i>	-From the shoulder to the hand to the shoulder on both arms.	12X	1 min
Administration	Twice per day		
Total/day			30 min

Appendix 3E: Multi-oral + tactile/kinesthetic stimulation

Fucile et al. (2002), Field et al. (1986)

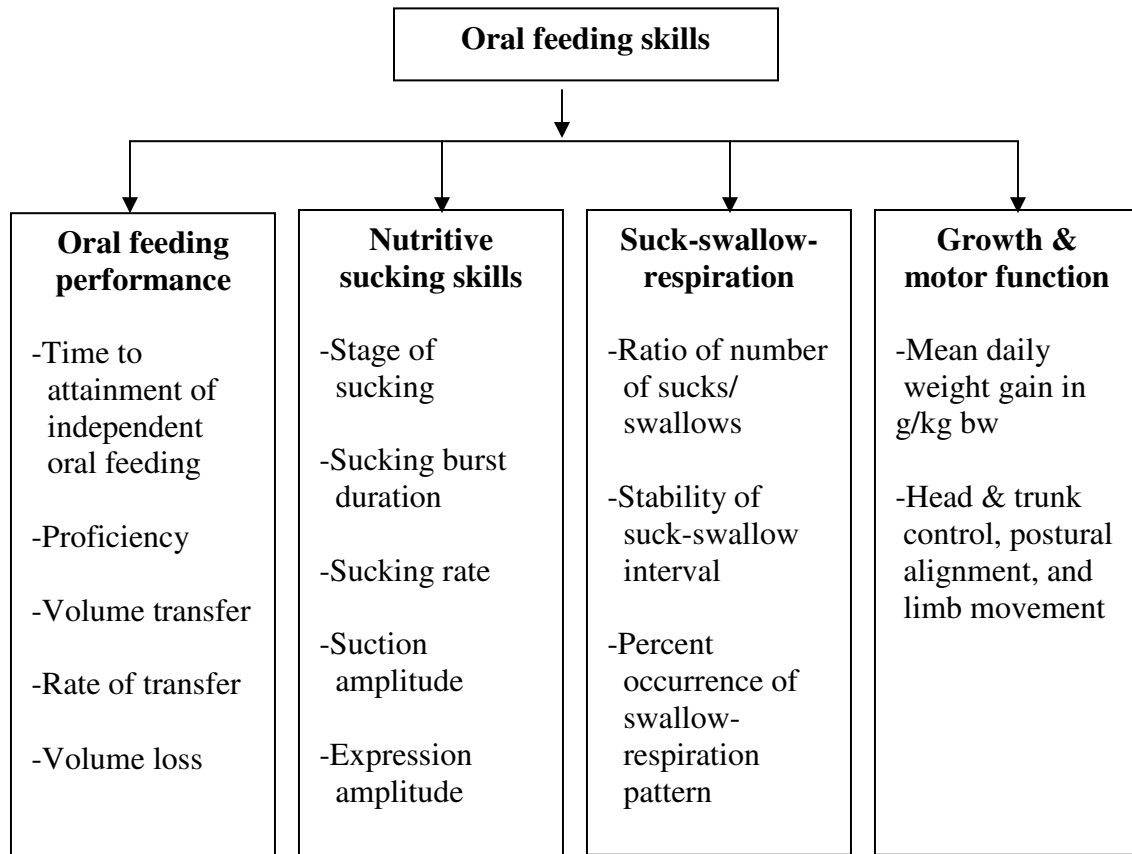
Characteristics	Stimulation Steps	Frequency	Duration
Peri-oral	Infant in supine position		
<i>Cheeks</i>	-Place index finger at base of the nose. -Move finger toward the ear, then down and towards the corner of the lip (C pattern).	4X each side	2 min
<i>Upper-lower lip</i>	-Place index finger at corner of the upper/lower lip. -Move the finger away, in a circular motion, from the corner towards the center and to the other corner.	4X each lip	2 min
<i>Upper-lower lip curl</i>	-Place index finger at center of upper/lower lip. -Apply sustained pressure, downward towards the middle.	4X each lip	2 min
<i>Jaw</i>	-Place index finger at hyoid bone. -Apply sustained pressure upward towards the chin tip.	4X	1 min
Intra-oral	Infant in supine position		
<i>Internal cheek</i>	-Place index finger at inner corner of lip. -Move back towards the molars, return to corner of lip.	4X each side	2 min
<i>Upper-lower gum</i>	-Place finger at the center of the gum, slowly move towards the back of the mouth. -Return to the center of the mouth.	4X each side	2 min
<i>Mid-blade of the tongue</i>	-Place finger at the center of the mouth. -Apply sustained pressure in the hard palate for 3 secs. -Move the finger down to the center blade of the tongue. -Displace the tongue downward with a firm pressure. -Immediately move the finger to contact the center of the mouth at the hard palate.	4X	1 min
Nonnutritive sucking	Infant in supine position		
<i>Pacifier</i>	-Place pacifier in mouth.	NA	3 min
Tactile	Infant in prone position. Stroke with your hands		
<i>Head-Neck</i>	-From the top of the head to the neck.	12X	1 min
<i>Neck-Shoulders</i>	-From the neck across the shoulders.	12X	1 min
<i>Back</i>	-From the upper back to the waist.	12X	1 min
<i>Legs</i>	-From the thigh to the foot to the thigh on both legs.	12X	1 min
<i>Arms</i>	-From the shoulder to the hand to the shoulder on both arms.	12X	1 min
Kinesthetic	Infant in supine position. With a firm grasp starting in neutral		
<i>Right Arm</i>	-Passive flexion & extension.	6X	1 min
<i>Left Arm</i>	-Passive flexion & extension.	6X	1 min
<i>Right Leg</i>	-Passive flexion & extension.	6X	1 min
<i>Left Leg</i>	-Passive flexion & extension.	6X	1 min
<i>Both Legs</i>	-Passive flexion & extension.	6X	1 min
Tactile	Infant in prone position. Stroke with your hands		
<i>Head-Neck</i>	-From the top of the head to the neck.	12X	1 min
<i>Neck-Shoulders</i>	-From the neck across the shoulders.	12X	1 min
<i>Back</i>	-From the upper back to the waist.	12X	1 min
<i>Legs</i>	-From the thigh to the foot to the thigh on both legs.	12X	1 min
<i>Arms</i>	-From the shoulder to the hand to the shoulder on both arms.	12X	1 min
Administration	Each once per day		
Total/day			30 min

Appendix 3F: Control intervention

Fucile et al. (2002). J Pediatr 141(2), 230-236.

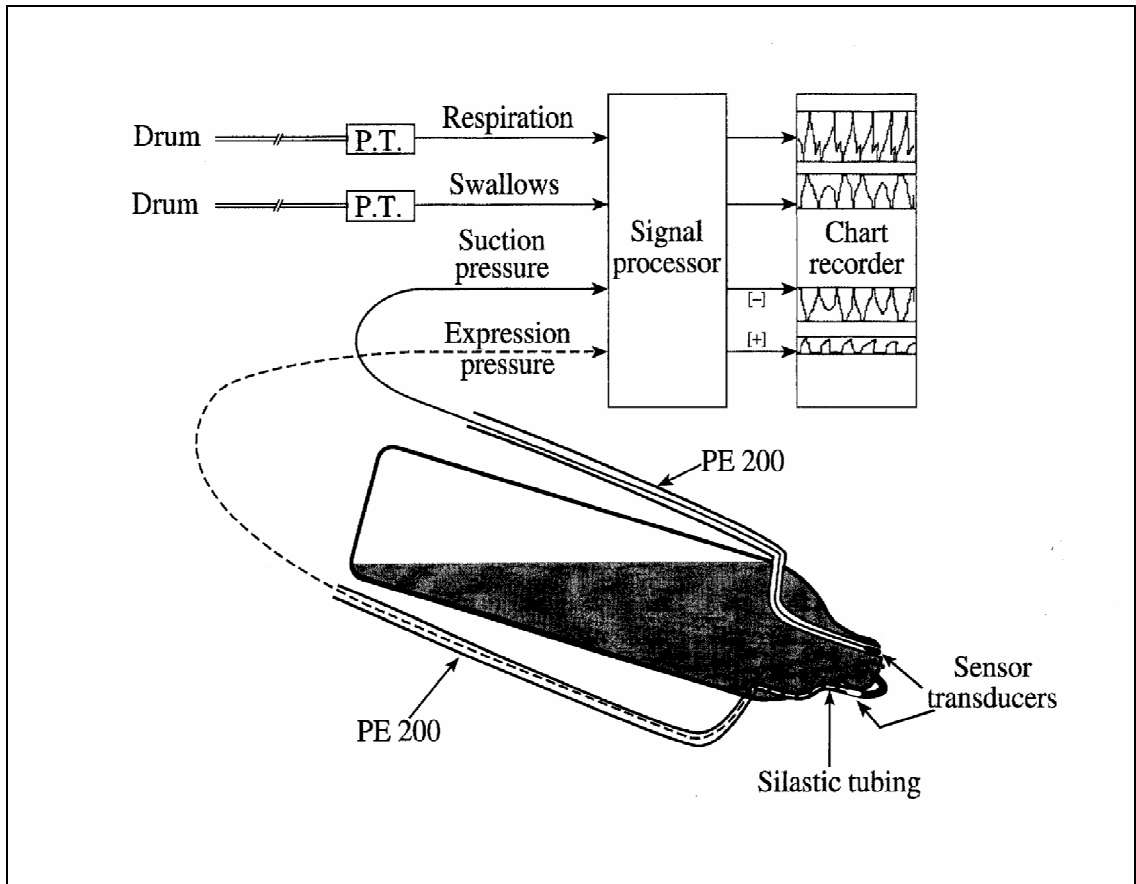
Characteristics	Stimulation Steps	Frequency	Duration
Control	Infant in supine position		
NA	-Place hands in isolette. -Observe the infant.	NA	15 min
Administration	Twice per day		
Total/day			30 min

Appendix 3G: Outcome variables



Appendix 3H: Nipple bottle apparatus

Lau & Schanler (1996), Clin Perinatol 23(2), 161-178.



PT-pressure transducer, PE-polyethylene tubing

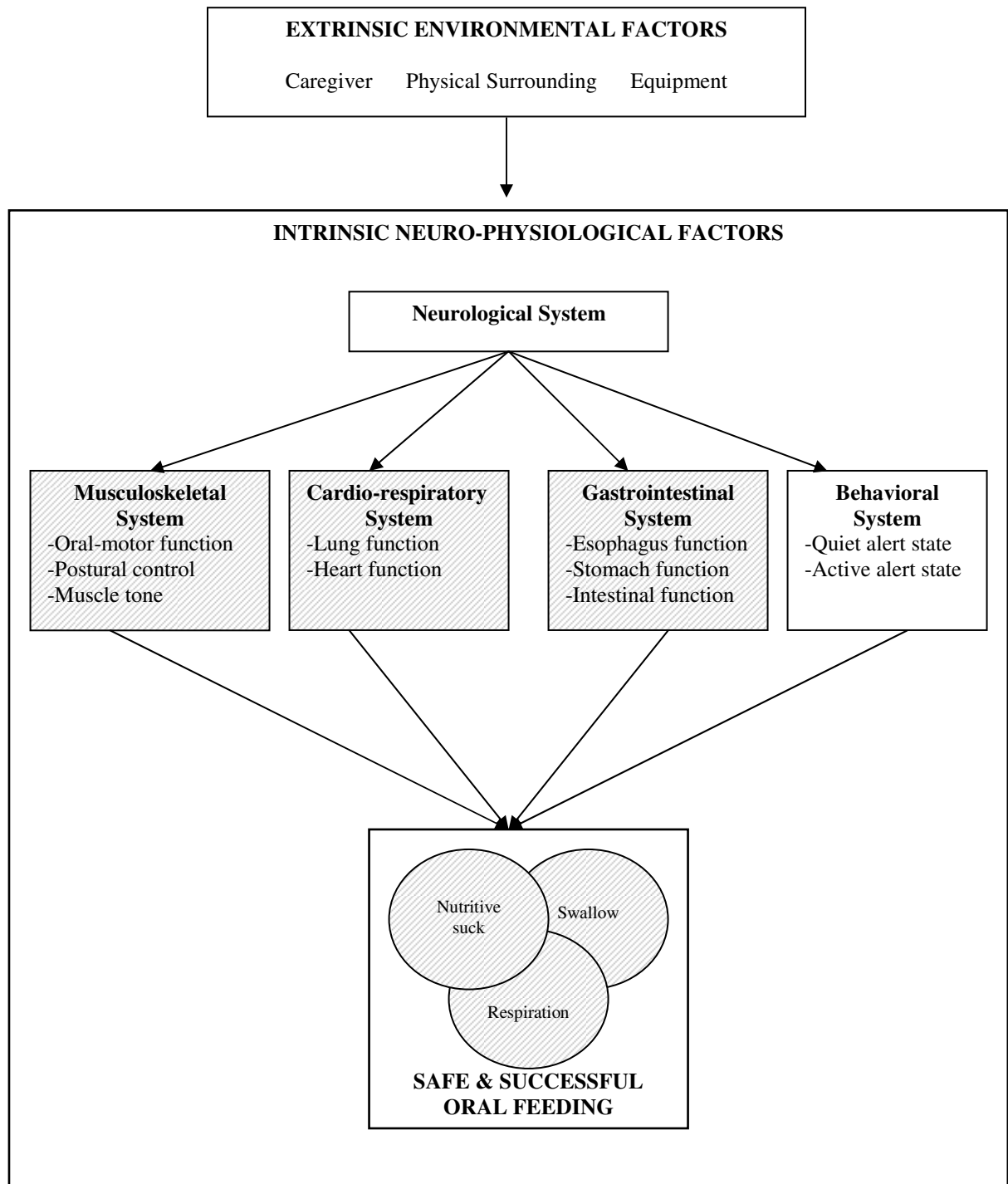
The nipple bottle apparatus allows for the simultaneous recording of suction and expression components of sucking, swallowing, and respiration. The suction component is monitored from a Mikro-tip sensor transducer (PE 200, model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a catheter flush with the tip of the nipple. The expression component is monitored via another Mikro-tip sensor (PE 200, model SPR-524, Miller Instruments, Houston, TX, USA) inserted through a silastic tube to 0.5 cm from the tip of the nipple. Swallowing is monitored via a small drum held snugly over the hyoid region. Swallowing causes an upward movement of the hyoid bone resulting in a pressure change inside the drum, and is recorded as a biphasic wave with an initial positive or negative pressure change. Respiratory effort is monitored via a drum (15 mm in diameter) taped in the midline at the thoraco-abdominal junction. This measure relates to changes in lung inflation as measured by chest and abdominal movements. All the transducers are connected to a Biopac MP 100 WSP system (Biopac Systems, Inc., Santa Barbara, CA), which is linked to a laptop computer. Data are stored for later analyses using the Acqknowledge software program included with the Biopac system.


Appendix 8A: Summary of findings

Outcomes	Uni-Oral	Uni-Tactile/ Kinesthetic	Multi-O+T/K	Control
Oral feeding performance				
Independent oral feeding (days)	√	√	√	
Proficiency (%)	√	√	√	
Volume transfer (%)	√	√	√	
Rate of transfer (ml/min)	√		√	
Volume loss (ml)	√			
Nutritive sucking skills				
Stages of sucking	√			
Sucking burst duration (s)				
Sucking rate (No. sucks/s)				
Suction amplitude (mmHg)	√			
Expression amplitude (mmHg)	√			
Suck-swallow-respiration				
Suck/swallow ratio				
Suck-swallow interval				
Swallow-respiration pattern				
Start I-Sw-End E				
I-Sw-I				
End I-Sw-Start E				
E-Sw-E		√	√	
Sw interrupt I				
Sw interrupt E				
P-Sw-P	√	√	√	
Growth & Motor function				
Weight gain before stimulation				
Weight gain during stimulation	√		√	
Weight gain after stimulation				
Motor function after stimulation		√	√	

√-significant effect, I-inspiration, Sw-swallow, E-expiration, P-pause

Appendix 8B: Oral feeding model & underlying systems



 -Shaded areas represent underlying mechanism/systems explored directly and/or indirectly in this study.

Appendix 8C: System specific sensorimotor inputs

