LATTA, JONATHAN A., M.A. Predicting Child Handedness from Measures of Infant and Toddler Handedness. (2020)
Directed by Dr. George F. Michel. 72 pp.

Cascade theory states that the development of hand preference for a simple action early in infancy will influence subsequent development of hand preference for more complex actions. To evaluate cascade theory, this study analyzed the relation of preferences across three age periods: infancy (6-14 months old), early toddlerhood (18-24 months old) and the preschool period (at 5 years).

The infant's manual preference for acquiring objects was assessed monthly across the 6-14-month age period and preferences were determined using a latent class model. This was compared to their manual preference for role-differentiated bimanual manipulation (RDBM) assessed during the 18-24-month age-period and finally these two preferences are compared to hand preference for RDBM at 5 years and differences in speed between hands when performing a one-handed peg-moving task that is commonly used to assess handedness at 5 years of age.

In all three comparisons, the classifications of hand preference significantly agreed with each other in a kappa analysis and failed to significantly disagree with each other when analyzed with a McNemar-Bowker test of symmetry. At age 5, the peg-moving task scores of the groups showing a preference earlier in development were significantly different from each other. The results are discussed in relation to the predictions of cascade theory.

PREDICTING CHILD HANDEDNESS FROM MEASURES OF INFANT AND TODDLER HANDEDNESS

by

Jonathan A. Latta

A Thesis Submitted to
the Faculty of The Graduate School at
The University of North Carolina at Greensboro
in Partial Fulfillment
of the Requirements for the Degree
Master of Arts

Greensboro
2020

Approved by

____
Committee Chair

APPROVAL PAGE

This thesis written by JONATHAN A. LATTA has been approved by the following committee of the Faculty of The Graduate School at The University of North Carolina at Greensboro.

Committee Chair ______________________________________

Committee Members ______________________________________

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Date of Acceptance by Committee

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Date of Final Oral Examination

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CHAPTER I

INTRODUCTION

1. Types of Asymmetry

A preference for one limb when performing a task is a trait shared not only by a vast majority of modern humans, but also by many other vertebrate species. However, when discussing motor asymmetry, there are important distinctions between individual-level asymmetry and population-level asymmetry. In individual-level asymmetry, individuals in a population prefer to interact with object in their environments using either their left or right limbs. If a species exhibits only individual-level asymmetry, which limb is preferred varies from individual to individual, with no bias observed at a population level. Population-level asymmetry, then, is a bias observed when most members of a species prefer to use one limb (sometimes the right or sometimes the left, depending on the species) rather than the species displaying a random or equal distribution of right and left preference. For instance, roughly 90% of humans have a preference for using their right hands for activities that clearly require the selection of one hand, such as writing or throwing (Corballis, 2009).

With evidence pointing to a clear population-level bias for manual actions in humans, the question of the evolutionary origins of this bias arises. At what point in the evolutionary history of *homo sapiens* does this bias emerge and which other phylogenetically related species exhibit similar patterns of behavior? Different studies have assessed limb preference in several primate species and several mammalian species and some of these studies have been examined using meta-analyses. The results create a somewhat confusing, but nonetheless informative, picture of the emergence of population-level limb preference in humans. However, before examining these comparative studies of limb preference, it is important that we define handedness in humans.

2. The Assessment of Hand Preference

Hand preference has been informally described as the bias for the preferred use of one hand over the other when performing unimanual tasks like writing, but this preference is not always consistent when multiple manual actions with objects are included in the analysis (Annett, 1970). Rather than being neatly divided into left- and right-handed groups, any given group of individuals may exhibit considerable variation in hand preference across tasks. This raises the critical question of exactly how to define a preference for using one hand over the other. Unfortunately, the operational definition of hand preference is a troublesome topic even among experts in the field. In order to assign a participant to a handedness group, each study must use some sort of decision criterion. Many handedness studies utilize a variation of a “Handedness Index” or “Laterality Quotient”, commonly defined as (Right-Left)/(Right+Left), which yields a score from -1 to +1 (Fagard & Marks, 2000; Esseily, Jaquet & Fagard, 2011; Campbell et al., 2015; de Vries et al., 2001). Positive scores on these types of scales typically indicate a right-hand preference, and negative scores indicate a left-hand preference. A key weakness of a handedness index or similar measure as a decision criterion is the relatively arbitrary cutoff points used to define the preference for one hand over the other. Using statistically defined criteria which identify the probability that the difference between the two hands is unlikely to have occurred by chance, removes some of the arbitrariness of the decision and ought to increase reliability of the assessment (Campbell, Marcinowski, Latta, & Michel, 2015).

When using a proportion-based laterality or handedness index, the total number of manual actions involved in the index must be considered in the formula. An individual who performs 7 out of 10 actions with their right hand and 3 with their left would have the same laterality index score as someone who performs 70 out of 100 actions with their right hand and 30 with their left although the score derived from the larger number of actions represents more information concerning the reliability of the assessment measure. In this example, a traditional HI measure would give this individual an index score of .4, indicating greater use of the right hand. However, this measure tells us little else about the nature of the observed manual actions or about the participant performing them. Can this individual be classified as right-handed? Were a sufficient number of trials run in order to determine anything useful about their hand use patterns? Also, when using an index-based measure of handedness, the researcher must arbitrarily select a cutoff point in order to distinguish preference for a hand. Is an index score of 0.5 sufficient to declare hand preference? Is it instead preferable to use a more conservative score of 0.75? These difficult decisions must be made when using index-based measures, and there is little support for the efficacy of any of these arbitrary cutoff points for defining preference. Using a measure that includes statistical significance or the likelihood of misclassification for determining hand preference (for instance, a z-score or a binomial test) is much more useful and defensible, as it provides a relatively non-arbitrary standard with which to make assignments of hand preference. Unfortunately, as I note in the next section, measures of limb-use in non-human animals also suffer from a lack of attention to how a preference is defined.

3. Assessment of Handedness in Non-Human Species

Chimpanzees (*pan troglodytes)*, a closely related to humans great ape species, have been shown in to exhibit a right-hand preference for several unimanual tasks, but across the observed sample, this preference was not as pronounced as in humans, with only 65% of the sample displaying a preference for throwing with their right hand (Hopkins et al., 2005). However, other studies provide contrasting results, finding either no population-level preference or suggesting that this preference is only displayed by chimpanzees in captivity and not by those observed in the wild (Harrison & Nystrom, 2008; McGrew and Marchant, 2001). Two meta-analyses of these small-sample studies support a pronounced right-shifted population-level preference for chimpanzees (Hopkins, 2006; Papademetriou, Sheu & Michel, 2005). Additionally, both of these meta-analyses use a z-score based criterion for determining hand preference which, as mentioned previously, is more statistically defensible for categorizing handedness. In an analysis of both a simple reaching (unimanual) and a stick-in-tube (bimanual) task, chimpanzees showed consistency of hand preference across their one-year age and their ten-year age but were found to deviate when reassessed at eleven years of age. (Padrell, Gomez-Martinez & Llorente, 2019). Moreover, the Padrell, et al. (2019) study also failed to find a population-level hand preference bias for chimpanzees for both unimanual (picking up food from the floor) or role-differentiated bimanual (using a stick to dislodge food from a tube) tasks.

Hand preference has also been assessed in bonobos (*Pan paniscus*), another great ape species closely related to humans. These studies of bonobos have produced mixed results with some showing a right-shifted population-level preference (Shafer, 1997) and others showing none (Harrison & Nystrom, 2008). The evolutionary conclusions drawn from these studies vary with their results, ranging from concluding that handedness emerged following the split of the *Pan* and *Homo* genera when no population-level preference is found (Harrison & Nystrom, 2008) to suggesting that adaptation to tool use influenced the development of human hand preference when evidence pointing to population-level preference is found in both chimpanzees and bonobos (Hopkins, Reamer, Mareno & Schapiro, 2015).

Hand preference (or paw preference in this case) has also been assessed in a variety of lab mouse (the C57BL/6J) that has been inbred for more than 120 generations to minimize the genetic variability in the sample (Collins 1968; 1970). First, the mice were deprived of food to motivate them. The hungry mice were then introduced into environments with narrow, cylindrical openings that would require the mouse to reach into them with one paw in order to get food. The paw selection for 50 actions was recorded and preference was categorized according to the individual mouse's RPE (Right Paw Entries) scores. These scores ranged from 0 (exclusive left-paw use) to 50 (exclusive right-paw use). Mice were classified as dextral (right-preferent) with a score above 25 and sinistral (left-preferent) with a score below 25. Females that displayed a preference did so much more strongly than their male counterparts, regardless of whether the preference was for their right or left paw.

The preference scores for these mice at the individual level were shown to be extremely reliable, with initial scores correlating with the 4-day and 1-month retest scores very highly (4-day correlations averaged 0.91 with 16 trials, monthly correlations averaged 0.98 with 100 trials). When compared to the right-shifted distribution of human hand preference, the distribution of mouse preference as presented by Collins is much more evenly spread. However, the shape of the distribution is quite unique, with many more strongly left-pawed and strongly right-pawed individuals than those with a less pronounced preference. This bimodal shape is roughly symmetrical, with no significant bias toward preference for the left or the right paw. This is a prime example of a species that displays considerable individual level lateralization of motor function while displaying no population-level bias. Also, since all members of the strain have nearly identical genotypes, the hand preference is unlikely to be related to their genotype.

4. Assessment of Handedness in Humans

There have been several common techniques for assessing handedness in humans: 1) Self-assignment - asking the person what their handedness is; 2) Questionnaire - asking people to indicate the hand they use for a number of manual tasks (the items on the questionnaire can vary from 10 to 60 and the answers can vary from "right, left, or either" to a 5- or 7-point scale ranging from "always left to always right"; 3) Observation – recording hand-use during the performance of common manual actions either in daily activities or in laboratory settings; 4) Proficiency tasks – measuring skill differences (latency, speed, accuracy, and/or duration). between the hands in performing unpracticed actions that are supposed to have limited overlap with commonly practiced skills. Each of these assessment measures have weaknesses.

Too many studies that are designed to examine the relation of handedness to other characteristics (e.g., intelligence, personality, various cognitive and social abilities, neural structures or damage) use the least valid measure – self-assignment. This assessment shows weak association with observational or proficiency measures. Therefore, I will discuss the other assessment techniques.

4.1 Questionnaire-Based Assessment

Over the last several decades, hand preference has been assessed in a variety of ways. In adults, the most common method of handedness assessment is to use one of the many available self-report questionnaires. Among the most widely used questionnaires are the Edinburgh Handedness Inventory (EHI) (Oldfield, 1971) and the Waterloo Handedness Questionnaire (WHQ) (Steenhuis and Bryden, 1989). Questionnaires like these present the participant with questions concerning a variety of everyday tasks for which one hand is selected over the other and elicit a self-report of hand preference for these tasks.

The EHI uses ten scenarios such as cutting with scissors, throwing, and striking a match for which the participant answers on a 5-point scale which hand they prefer to use for each task and the strength with which they prefer to use it. In the columns corresponding to each hand, a "++" in one column is used to signify strong preference for one hand, "+" is used to signify moderate preference for one hand, and a "+" in each hand column signifies no preference for that specific task. Classifying individuals into different handedness categories is not done statistically but rather by the researcher's decision. Sometimes the scores are not classified but are allowed to vary continuously for the purposes of correlating them with other measures. Many revisions have been made to the EHI since its introduction but without concerns for either consistency with other EHI studies or even an explanation for the revision (Edlin et al, 2015). Also, the

EHI has been criticized for using common western tool tasks for which individuals will likely have received deliberate instruction for use or could have derived use from imitating parents or other adults (Michel, Nelson, Babik, Campbell, & Marcinowski, 2013). Finally, Oldfield, who created the EHI, noted in his publication of the scale that it was to be used for quick clinical evaluations but not for research purposes, stating that there are situations in which a behavioral measure of hand preference is "essential." (Oldfield, 1971).

The WHQ uses a similar set of questions, but increases their number to between 15 and 60, depending on the version used (Steenhuis and Bryden, 1989). The WHQ uses a similar scale to the EHI, from -2 (Always Left) to +2 (Always Right) to assess hand use for a variety of everyday tasks. The revised version of this assessment, when complete, yields a narrower score range of -40 to +40. Analyses of the relationship between hand preference assessed with a questionnaire and measures of proficiency have provided somewhat mixed results. When analyzed with three different levels of task complexity, tapping speed and accuracy correlated poorly (according to the authors despite the r values) with an EHI-like task-based questionnaire of hand preference, with the correlation decreasing as the difficulty of the proficiency task increased. ($r=.733$, .689, and .619) (Todor & Doane, 1977). A study written by one of the co-creators of the WHQ contrasts in its findings with these results, instead suggesting that the results from their Waterloo Questionnaire and their WatHand Box Test (a proficiency based measure) correlate significantly ($r=.321$, $p<.05$) (Cavill & Bryden, 2003). It is notable that the Cavill and Bryden study found a correlation of .32 significant and reliable while Todor and Doane considered much more robust r values to be weakly correlated.

Assessing handedness is much more difficult in children, given their relatively lower capacity for verbal expression and comprehension. Methods that are commonly used with adults such as self-report and questionnaires become impractical and ineffective when applied to children. Also, proficiency assessment techniques require participants to comprehend and follow the researcher's instructions and to be motivated to perform well, pre-requisites that may be lacking or reduced in young children. Therefore, observational methods are preferred when assessing handedness of infants and young children because directly observing hand use allows researchers to measure the child's hand preference without needing verbal input from either the child or relying on a second-hand report from a guardian. Many of the observational methods used for studying child handedness use a controlled laboratory or home setting in which the children are presented with objects that elicit a specific manual behavior of interest (Michel et al., 2013, Campbell et al., 2015, Esseily et al., 2011). As children develop, they become capable of performing increasingly complex manual actions, which can be assessed for hand preference.

4.2 Observation-Based Assessment

Observational studies often study a specific set of manual actions, progressing in complexity from simple behaviors such as pointing and reaching (Jacquet, Esseily, Rider

& Fagard, 2012) to grasping and unimanual manipulation (Campbell et al., 2015) to complex coordinated behaviors such as Role-Differentiated Bimanual Manipulation (RDBM), object-construction, and tool use (Kimmerle, Ferre, Kotwicka & Michel, 2010; Marcinowski, Campbell, Faldowski & Michel, 2016) Typically, these observational assessments consist of video-recorded structured play in which the child is presented with one object at a time in a consistent manner and hand use is tallied by a coder. Naturally, each of these various behaviors requires unique play scenarios and manipulated objects to elicit the desired actions. For instance, pointing and reaching can use a wide variety of simple objects such as figurines or rattles to elicit actions from the infant. More complex behaviors require the use of toys that afford such behaviors, including multi-part toys, containers, or specifically designed tasks for tool use.

To ensure consistency across children, these observational methods use a consistent set of objects, usually toys, ranging in number from fewer than ten (Esseily et al., 2011, Rat-Fischer, O'Regan & Fagard, 2013) to more than thirty (Michel et al., 2013; Michel, Ovrut & Harkins, 1985). There has been some disagreement among researchers concerning the effect of the number of presented items on the resulting handedness classification of the tested child. An analysis of disparate methods (one using 9 presentations, the other using 32 presentations) determined that when analyzing the same children monthly across the 8-14 month time window, the two assessment techniques yielded significant differences not only in their monthly assignment of children to a hand preference group, but also in the resulting latent classes when analyzed using group-based trajectory modeling (Campbell et al., 2015). A reaction study was done looking at the influence of the number of trials involved in assessing infant handedness (Fagard et al., 2017). This study measured the handedness group assigned to each infant using 5, 10, 15, 20, 26, 31, and 34 trials. Using this method, Fagard and colleagues found that after 15 trials, additional trials added no change in the significance of the correlation. However, this study used progressive (5, 10, 15, etc.) subsets of the existing manual action data, with all subsets being taken from the same 34-trial task. Naturally, any subset of data will correlate with the full set, with that correlation approaching 1 as the size of the subset approaches the size of the full set. This is particularly true when the subsets are progressive. Therefore, the 15-trial conclusion is weakened; it would have been better to have compared two separate presentations, as in the Campbell, et al. study.

4.3 Proficiency-Based Assessment

There are also assessments that instead of examining differential frequency of hand use, use the difference in speed or proficiency between the hands when performing a task to assess preference. Among these are the Annett Peg-Moving task (Annett, 1970) (used in the current project) and the Tapley-Bryden dot-marking task (Tapley & Bryden, 1985). In the Annett peg-moving task, ten pegs are moved from the top row of an apparatus to the bottom as fast as possible in order to determine the difference in proficiency between the left and right hands. The difference in speed between the two hands is used as a measure of preference with the faster hand being the preferred one. Accuracy is assured by requiring the peg to stay in the hole to which it is moved.

The Tapley-Bryden dot-marking task features a series of small circles or ovals laid out in a serpentine fashion. Using a pen or marker, the participant must make a mark inside each of the circles in sequence as fast as possible in a set time period. The number of circles successfully marked with the left and right hands in the allotted time is recorded, and rather than use the time differential between the hands as a measure of preference as in the difference in the number of successful marks between the two hands is used as a measure of preference. Accuracy is measured for a specific time frame. Hole-punching variants of the dot-marking tasks have also been used as a proficiency measure of hand preference (Annett, 1992). While these proficiency measures are not as commonly used as observational measures, they provide a complementary perspective of a process that is related to many other developing processes in the brain.

5. The Importance of Hand Preference

5.1 Hand Preference and Other Lateralized Functions

The lateralization of motor functions has been closely associated with several other lateralized functions, but the most prominent of these simultaneously developing functions is language. It has been theorized that language had its origins in hand gestures, which today are still universally used to communicate salient points (Hewes, 1973). A person may point to an object of interest in the distance to draw the attention of another or motion to beckon another individual to approach them. A hand may be held out flat to halt someone's approach or a finger may be held up to lips to communicate the need for silence. Even without any accompanying words or noise, these gestures have a clear meaning that can be communicated from one person to another or from one individual to a group. This theory suggests that language developed in a very different environment, with hominids surviving in a much more dangerous habitat. It has also been suggested that language has an adaptive function, such as it allowing for the use of both hands while still communicating (Corballis, 2010) but also suggests that early language would have been much simpler than current languages, lacking the nuance and depth that languages now possess.

Hewes suggested that commonly used spatial hand gestures became standardized over time and across groups, and that these hand gestures were eventually converted into sounds (a process called glottogenesis). Similarly, these sounds were standardized and spread through contact with other groups. However, Hewes made no suggestions as to how the process of glottogenesis occurred. Hewes and others point to the fact that gestural language is much more easily acquired by primate species than speech as support for the notion that speech is descended from gestural communication. Also, facial gestures can be used to augment the meaning associated with spoken language. Smiles and frowns are common facial gestures that add an additional layer of meaning to our communication, possibly even changing its meaning entirely. Studies of monkeys show that the same area of the brain (F5, analogous to a portion of Broca's area in the human brain which is associated with the production of speech) activates when the monkey is presented with gestural signals or facial signals, suggesting that both are effective forms of communication for the primate (Corballis, 2010).

If verbal communication was derived from manual gestural communication, then it follows that the development of hand use would be developmentally linked to the development of language skills. The literature seems to support the notion that the development of hand use and the development of language are closely related. Infants that displayed a right-hand preference and that were consistent in that preference from infancy (6-14 months) to toddlerhood (18-24 months) scored higher at 24 months on the language domain of the Bayley Scales of Infant and Toddler Development (Nelson, Campbell & Michel, 2014). As a group, right-handers have been shown to demonstrate different lateralization patterns for language than left-handers (Szaflarski et al., 2012). Rather than being a mirror image of their right-handed counterparts, the left-handed group showed less of a shift toward left-hemisphere activation when presented with a language task as assessed by fMRI. When examining the frontal lobes, a majority of the left-handers (85%) still showed language-related activation in the left hemisphere, with 11% displaying symmetrical activation and 4% displaying right-hemisphere activation. Right-handers were much more left-shifted in their frontal lobe language activation, with 93% showing left-hemisphere activation, 6% symmetrical, and 2% right-hemisphere activation. Temporo-parietal differences were much more pronounced, with left-handers showing only 67% left-hemisphere activation, 22% symmetrical, and 11% right-hemisphere activation, compared to a right-handed group that showed 91% left-hemisphere activation, 7% symmetrical, and 2% right-hemisphere activation.

Similarly, a transcranial sonographic study of speech found differences in the location of the frontal lobe activity associated with language between left- and right-handers (Knecht et al., 2000). This study found a strong relationship between strength of handedness and percentage of the sample showing right-hemisphere dominance for language. This percentage of right-dominance was also nearly linear across the handedness groups. Extreme (-99 and less on the EHI) left-handers displayed 27% right-hemisphere language dominance, as did the strong (between -99 and -75 on the EHI) left-handers. Weak (between -75 and -22 on the EHI) left-handers showed 22% right hemisphere dominance for language. Those showing no preference (between -25 and +25 on the EHI) showed 11% right hemisphere dominance. Weak (+25 to +75) right-handers showed 10%, strong (+75 to +99) right handers showed 6%, and extreme (+99 and higher) right-handers showed 4%. Note that the Knecht, et al. study inappropriately used the EHI for their research. While these differences in lateralization of activation are striking, the vast majority of the samples in both of the studies remained consistent with the more common patterns of speech lateralization, with most of the activity remaining in the left hemisphere.

Also, both of these studies use bloodflow-related definitions of brain activity. FMRI measures the volume of blood flow to a particular area in the brain combined with the oxygen metabolism in that area using a measure called the BOLD (Blood Oxygen Level-Dependent) signal (Ekstrom, 2009) and transcranial ultrasound relies on shifts in the speed of laminar blood flow inside the blood vessels of the brain area of interest (Purkayastha, 2013). These indirect measures of brain activity, particularly fMRI, are increasingly common when discussing the association of behavior and brain activity, and the connection between these measures and the actual firing of neurons is less direct than many of these studies would suggest. The prevailing theoretical model of the representative properties of the BOLD signal couples the BOLD signal with “local field potential” or the electrical activity surrounding the synapses in the area of interest. This theoretical connection is referred to as the BOLD-LFP model.

There are scenarios where the electrical activity in the brain and the BOLD signal are not in agreement, which raises questions about the validity of the relationship as a measure of neural activity and about the widespread reliance on this measure to associate neural activity and behavior. Such scenarios include a dissociation of neural spiking activity and the associated BOLD signal seen in the parahippocampal area during an interactive spatial/perceptual task (Ekstrom, Suthana, Millett, Fried & Bookheimer, 2009). The study of 6 individuals used implanted depth electrodes in patients with epilepsy to monitor electrical activity while the patients explored a virtual world. In this scenario, there was no relationship found between the neural firing rate in either the hippocampus or the parahippocampal region and the strength of the BOLD signal associated with the activity.

These divergences of BOLD and neural activity are found in animal models, as well. In a rat model, Angenstein and colleagues (2009) found inconsistent BOLD responses to different levels of direct hippocampal stimulation, with early trials showing that direct stimulation of the hippocampus increased neural spiking activity in the dentate gyrus but decreased BOLD signal. Later trials showed the opposite effect, with the same direct stimulation decreasing spiking activity but eliciting an increase in BOLD signal. While these inconsistencies certainly do not completely devalue or invalidate the use of these methods to study brain activity and its relationship to behavior, it highlights the need for caution and stresses the importance of understanding what exactly is being measured in these studies.

5.2 Hand Preference and Psychopathology

Hand preference has also been linked with differences in the incidence of a wide variety of psychopathologies. In men, a higher prevalence of non-right-handedness was found in a schizophrenic sample when compared with a non-schizophrenic control group. (Sperling, Martus & Barocka, 1999). In this study, rather than compare left-handers to right-handers, the authors chose to compare right-handers to any non-right hand use for creating a preference classification. This relationship was not found in the female portion of the sample. Another investigation into the relationship between hand preference and schizophrenia found that in schizophrenic patients, non-right-handed males were found to have larger cerebral ventricles than their right-handed counterparts (O'Callaghan, 1995). This study also found that non-right-handed schizophrenic females scored significantly lower than the right-handed female portion of the sample on a battery of cognitive tests that included the Wechsler Adult Intelligence Scales and the National Adult Reading Test. Both of the aforementioned studies used questionnaire-based assessments (one used the Shimizu-Endo, a weighted questionnaire similar to the EHI and the other used the EHI) to assign their samples to right- and non-right-handed groups.

In a sample of children with fetal alcohol syndrome (FAS), a much higher incidence of disruption of lateralization was seen in both motor function and in auditory function (Domellöf, Rönnqvist, Titran, Esseily & Fagard., 2009). Compared to controls, these children, ranging in age from 5 to 17, demonstrated a much higher proportion of non-right-handedness. (30.4% compared to 13.2% from the control group.) However, other motor modalities such as eye or foot preference did not show this shift in bias. In a dichotic listening task in which different information is presented to each ear simultaneously, a majority of the control group (92.9%) displayed a marked preference for the information presented for the right ear. In contrast, the FAS sample did not display this same preference, instead preferring the left ear as a group by a narrow margin (52.5% vs the 7.1% from the control group preferring left ear information).

A similar result was seen when analyzing the relationship between hand preference and Down syndrome (Groen, Yasin, Laws, Barry & Bishop, 2007). The children, all between the ages of 7 and 13, were assessed for hand preference using two methods, one a simple behavioral observation consisting of five presentations, and a second involving the presentation of cards in a semicircular arc around the child. Forty-three of these were normally developing and 30 children had been previously diagnosed with Down syndrome. A much greater percentage of the sample with Down syndrome (48.3%) displayed mixed or left handedness compared to a control sample (14%).

Rather than assigning any causal responsibility to either side of these relationships, Marian Annett (2008) suggests that both the psychopathology and the development of an unusual pattern of lateralization are secondary to other influences disturbing the growth process. A clear example of this is Fetal Alcohol Syndrome. The common phenotypic changes and cognitive impairment associated with this disorder are related to the changes in lateralization, but neither of these effects is causing the other. Instead, it is the prenatal exposure to the alcohol which has widespread teratogenic effects that include phenotypic, cognitive, and neurological changes.

6. The Developmental Origin of Hand Preference

6.1 Contrasting Theories of the Developmental Origin

Theories of the development of hand preference disagree on what causes this trait to appear. Some suggest that it is genetically determined (McManus, 1985), or that handedness emerges from unspecified maturational programs governing the development of lateral asymmetries of the brain (Fagard, 2006). Others have instead suggested that it is a byproduct of the genetic determination for left hemispheric control of language processes (Annett, 1985) or that it is an emergent property of postural development (Corbetta & Thelen, 1996; 2002). Still others believe that it is a trait consisting of a cascade of asymmetric manual biases, starting before birth, which influences the acquisition of manual skills as they develop during early childhood and which eventually becomes an aspect of individual identity (Michel, 2002). If this cascade theory is correct, then there should be a discernible path starting from early developmental manual asymmetries and leading to manual biases in the preschool child. For instance, according to this theory, a pre-school child that exhibits a preference for their left hand should have had a history of left-hand preference for increasingly complex tasks earlier in their development.

The genetic theory of the origin of hand preference has progressed from assigning responsibility to a single gene that causes the entire distribution of human handedness to shift toward a right-hand bias (Annett, 1998) to the suggestion of the existence of a multi-locus gene that attempts to explain this same shift (McManus, Davison, & Armour, 2013). A genome-wide association study (GWAS) was performed looking for the presence and location of the proposed single gene, but no strong association with handedness was found with any single gene (Armour, Davison &

McManus, 2013). However, the genetic theory persists and the debate as to the model that best fits the theory of the genetic transmission of hand preference goes on.

Lateralized motor behavior begins long before hand preference emerges, though there is some disagreement as to when this behavior can be reliably assessed. There are those that support the notion that prenatal behavior can be assessed and categorized for lateralization. For example, Hepper used of ultrasonic images to attempt to determine preference for arm movements and thumb-sucking behaviors in-utero (Hepper, Shahidullah & White, 1991). This study found that a large majority (80%) of fetuses sucked their right thumb at 15 weeks gestation. A follow-up study showed that the children that displayed a right-handed prenatal preference in the 1991 study had developed a right-hand preference when tested at 10-12 years of age (Hepper, Wells & Lynch, 2005). However, a later study examining lateralization of head orientation and of hand-head interactions in fetuses via ultrasound found no preference develops for unimanual actions across the 12 to 38-week gestational period (de Vries et al., 2001). This study did find the development of lateralization for head orientation with a bias toward the right side as gestation progressed from 30 to 36 weeks.

According to Michel's cascade theory, (Michel, 2002), hand preference is the result of a chain of lateralized behaviors that begins in prenatal development. This theory suggests that prenatal asymmetries such as orientation in the womb provide disparate opportunities for movement and self-stimulation to each of the limbs. If a fetus has greater freedom of movement with its right hand, for instance, then that difference in feedback experience with the movement of, and sensation from, that side will bias neuromotor development towards that side. Moreover, the fetus has a typical uterine orientation in which the head is frequently able to turn toward the right (with a minority of fetuses with a uterine orientation that results in more frequent head turns to the left) (Matsuo, Shimoya, Ushioda & Kimura, 2007). This early uterine bias results in differential development of the left and right vestibular systems (Previc, 1991) and is proposed to be manifested in the newborn supine head orientation preference (Goodwin & Michel, 1981; Michel, 1981). For the first 8-10 postnatal weeks, infants prefer to orient their heads to the right (with about 12% preferring a leftward orientation) when supine, seated, or cradled (Michel, 1981). This head orientation preference can differentially influence which hand gets more visual exposure and it promotes differential coordination of movement activity between the hands (Michel, 1981). These asymmetries of visual exposure and movement likely create neuromotor differences in how the hands' actions are controlled (Michel et al., 2013).

Subsequently, these early differences predict manual differences in swiping at visual targets at 3-4 postnatal months (Michel et al., 2013) and differences in object acquisition (grasping a toy and manipulating it in such a way that it is lifted from the surface of the table) at 5-6 postnatal months (Michel & Harkins, 1986). Object acquisition asymmetries cascade into later manual asymmetries in manipulation (performing specific actions with an object held in one hand) preferences (Campbell, Marcinowski, & Michel, 2015) and even later into preferences for role differentiated bimanual manipulation of objects (Babik & Michel, 2016a) and object construction skills, (Marcinowski et al., 2016). Cascade theory suggests that the development of hand preference for an emerging manual skill is the result of previously established hand preference for a manual skill that emerged earlier in development. In this manner, hand preferences accumulate across manual skills resulting in a consistent hand-use preference across skills.

6.2 Relationships Between Manual Actions

Previous research has found that hand preferences for object acquisition can be distinguished as early as 6 months of age (Campbell, Marcinowski & Michel, 2018). Using group-based trajectory analysis on monthly longitudinal object acquisition data collected from 380 infants from 6 to 14 postnatal months, four latent groups were identified: an early developing right-handed group (32%), a later developing right-handed group (25%), an early developing left-handed group (12%) and a group without a preference (30%) across this age period. By 10 months, a hand preference for unimanual manipulation of objects emerges and that preference is predicted from the acquisition preference (Campbell et al., 2015).

Infants develop more complex and demanding manual skills such as role-differentiated bimanual manipulation (RDBM) toward the end of their first postnatal year (Babik & Michel, 2016). In RDBM, one hand supports the other hand's exploration of an object. An example of role-differentiated bimanual manipulation would be peeling an orange: one hand holds the orange while the other pulls at the peel. The hand stabilizing the object or holding the orange is considered to be the non-preferred hand, while the hand performing the manipulations or peeling the orange is considered to be the preferred hand. The manipulating hand is considered to be the preferred hand because it is presumed that the task it performs in RDBM actions requires more dexterity and hand-eye coordination than the actions performed by the stabilizing hand. It was predicted by cascade theory that the hand preferred for acquisition and unimanual manipulation should begin to be preferred in their RDBM actions. Role-differentiated bimanual actions are a staple of handedness development research and have been used extensively as a measure of the lateralization of motor function in infants (Ramsey & Weber, 1986; Fagard & Jaquet, 1989). Hand preferences for RDBM begin to appear during the 12-14-month age period (Babik & Michel, 2016) but might not consolidate until later ages (Nelson, Campbell & Michel, 2013).

Longitudinal assessment of any sample of infants across several assessment periods introduces specific challenges to the gathering and analysis of the resulting data such as attrition, but also affords perspectives on development that cross-sectional designs fail to provide. The multiple data points for each infant can be used to construct a trajectory that tracks the development of their preference for a given behavior over time. Group-Based Trajectory Modeling (GBTM) allows the compilation of these individual trajectories into groups based on how well these trajectories collectively fit the proposed models (Nagin, 2005; see Michel, Babik, Sheu, and Campbell, 2013 for application to the study of handedness). These "latent classes" define groups of infants that show similar developmental trajectories (intercepts and slopes) across the age range of data collection.

Campbell and colleagues' examination of object acquisition (Campbell, Marcinowski, Babik & Michel, 2015) and unimanual manipulation and Babik and Michel's (2016) analysis of bimanual manipulation used GBTM to distinguish how many latent classes were associated with the development of their respective skills of interest. In order to create these latent classes, the infant's hand preference at each month must be assessed. In the Campbell, et al study of unimanual object manipulation and the Babik study of bimanual manipulation, handedness index scores were calculated using the infant's monthly left and right-handed acquisition actions for 30 objects using a standardized proportion of right-hand use known as a handedness index. This index assigns a more positive score to an infant with greater right-hand use, and a more negative score to an infant with greater left-hand use. These monthly scores are compiled across months to create a developmental trajectory for each infant. Then, the trajectories are collectively analyzed using group-based trajectory modeling to determine how many groups the data can be divided into with the least amount of total variance. One study (Koucheki, Campbell, & Michel, 2015) has shown the 6-14-month group to be broken into four latent classes (early right, late right, no preference, early left), while another (Michel et al., 2016) has shown that the 18-24-month group is also best divided into four groups (strong right, right, no preference, left).

In support of the cascade theory, Nelson, Campbell, and Michel (2013) demonstrated that a right-hand preference for object acquisition during infancy predicts a toddler's right-hand preference for RDBM across the 18-24-month period. Unfortunately, none of the toddlers in this study had exhibited a left-handed preference for acquisition. Because right hand preferences are predominant for both ages, this study does not provide adequate evidence for the cascade effect in which early left preference must predict later left preference. A replication with a larger, more diverse sample is needed to determine the existence of this effect. Also, while this study only represents three possible time points in what is thought to be an entire chain of developmental events, a replication study with more age groups represents a promising opportunity for the investigation of cascade theory.

This predictive connection between hand preferences in several early developing manual skills raises questions concerning the relation of hand preferences to other manual skills. There are measures of hand preference that are assessed much later in the child's life compared to when acquisition and unimanual skills emerge, but the literature is incomplete about how these later measures of handedness relate to the measures of early development. The goal of my thesis is to examine the relation between early handedness measures and later handedness by connecting measures of infant and toddler handedness to preschool child handedness. The present study examines the consistency of hand preference across childhood by examining the predictive relation of infant hand preference (object acquisition) and toddler hand preference (RDBM) to hand preference (for RDBM) and differential hand performance in a peg-moving task at 5 years of age. Cascade theory predicts that object acquisition handedness and role-differentiated bimanual manipulation handedness result in differences of hand preference and hand proficiency at five years old. Therefore, the hand preferences for object acquisition in infants and RDBM in toddlers each will predict 5-year preference as measured by both RDBM classification and differential hand performance on a peg-moving task.

CHAPTER II

METHOD

1. Participants

The participants are infants, toddlers, and 5-year-old children who were recruited for a longitudinal study of hand preference development. Our participants were recruited from birth records that were obtained from the Guilford County Courthouse in Greensboro, North Carolina. Informed consent was obtained from the parents at the beginning of each age-based cluster of visits (6-14 months, 18-24 months, and 5 years). Originally, 383 infants contributed to the study of infant hand-use preferences but the number of children who were seen at 5 years of age was only 58 as a result of attrition and the design of the study. These 58 5-year-old children were used to compare their hand preference for object acquisition as infants, and RDBM as toddlers and their performance on the peg moving task and their RDBM hand preferences as 5-year-olds. Of the children that were assessed in infancy, 42 children were also assessed with the Annett peg-moving task. Likewise, 43 of the children assessed across toddlerhood were assessed with the peg-moving task.

1.1 Demographics

The city of Greensboro, from which our sample was drawn, was 44.0% Caucasian, 41.4% African American, 7% Hispanic, 4.4% Asian, 0.4% “Some Other Race”, 2.1% belonging to “Two or More Races”, 0.3% American Indian or Alaska Native, and 0.1% Native Hawaiian or Pacific Islander. (U.S. Census Bureau, 2017). The original sample of 383 who completed the demographic survey (337 individuals) is shifted somewhat from these proportions, with a greater percentage of the sample being Caucasian, and a lower percentage of the sample being African American or Hispanic. 58.5% of the sample responded as White or Caucasian, 25.5% Black or African American, 3.0% Hispanic, 1.5% Asian, 0.3% Pacific Islander/Hawaiian, 7.1% multiracial, and 4.2% categorizing themselves as “Other”. The tested subsample of 58 is shifted further in the same direction. Of these 58 children, 43 (74.1%) were white, 9 (15.5%) were African American, 2 (3.4%) were Hispanic, 1 (1.7%) was categorized as “Other”, and 3 (5.2%) were multiracial. 33 (57%) of the children were male, and 25 (43%) were female. The full sample of 383 infants were used to identify the four latent classes for infant hand preference and 101 toddlers were used to identify the four latent classes for toddler RDBM hand preferences. Only the 58 infants and toddlers that were assessed at 5-years of age were analyzed for hand preference consistency in this study.

2. Materials

This longitudinal design was divided into three tasks, one for each age group. In order to examine object acquisition with the 6-14-month object acquisition group, the toys detailed in the Campbell, Marcinowski, Latta, and Michel (2015) 32-toy hand preference assessment task were used. These toys included a small xylophone, plastic chains, a ring on a string, etc. Depending on the design of the toy, it was either presented on the table or suspended in the air in front of the infant.

For the 18-24-month task, the hand use for the toys that afforded RDBM actions that were listed in the task from Nelson, Campbell, and Michel (2013) was recorded. This battery of 14 toys included toy cars with a figurine inside that allowed for the separation and reinsertion of the driver, a foam block with a round foam peg stuck inside that could be removed and reinserted, and a block with a window in the side that encouraged the manual exploration of moving parts inside. RDBM hand preference at 5-years of age was assessed with the same toys from the 18-24-month assessment.

The performance assessment of hand preference for our 5-year old sample compares the speed with which the child moves 10 pegs with each hand from one line of holes to another as fast as possible (Annett, 1970). The task involves sequentially moving ten pegs from the top rack to the bottom rack of a specially designed board as fast as possible for three times with each hand. The difference in average speed between left and right hands is used as a measure of differential proficiency between the two hands. For the 5-year peg-moving task, we used a specially designed apparatus that was constructed according to the specifications provided in Annett (1970). The apparatus consists of two boards, each drilled with 10 half-inch diameter holes 1 inch apart and 1 inch deep. These boards are connected by two perpendicular boards on the bottom, leaving 8 inches between the two rows of holes (Figure 5). The pegs used in the trials are ten 4” long x 1/2“ diameter dowels. Following Annett’s procedure, a digital stopwatch and a timesheet are used to record the time for the six (three for each hand) trials for each child. These trials were coded during the presentation by the presenter as the child moved the pegs from top to bottom, starting the timer when the child pulled the first peg out of the apparatus and stopping the timer when the tenth peg was placed in its hole.

For each of these three age groups, the interactions with the toys were recorded from above and from the left side using two video cameras (Panasonic WV-CP240) to prevent ambiguity in coding and used a video mixer to combine the two video streams into one. This stream was saved into a video file on a connected PC and saved for later coding. These files were coded using Noldus Observer (Version 11.5) software to provide the ability to slow down and to stop the presentations and to analyze them frame-by-frame when necessary. These videos were coded by the investigators and research assistants, with 20% of the videos recoded separately to measure inter- and intra-rater reliabilities.

3. Procedure

At the first visit of each of our visit age periods (6-14-months, 18-24-months, and 5 years), informed consent was obtained from the parents after explaining the experimental procedures and the recording process. The IRB at UNC Greensboro approved the consent form that the parents signed. At the 6-14-month visits, the child sat down, either on their parent’s lap or by themselves, in a chair in front of a semi-circular table that curves around them (Figure 6), giving the infant ample room to play in front of them and on both sides. Toys to assess acquisition were then presented to the infants either one at a time or in pairs and were placed on the table or held in the air, depending on the design of the toy. The toys were presented as close as possible to the infant's midline to prevent hand selection based on proximity.

For the toddler and 5-year RDBM presentations, the children sat at the semi-circular table in a manner similar to the acquisition presentations, although most 5-year-old children did not sit on their mothers' laps. The toys presented during these sessions are chosen for the RDBM actions that they afford, (like unzipping a bag or removing a ball that has been fastened to the inside of a tube). These actions are not possible to perform with a single hand. These toys were also presented to the child's midline to avoid any proximity bias for hand-use. The time when the participant performed the desired action and the hand they used to perform the active portion of the RDBM were both recorded.

Also, at the 5-year visits, the relative performance proficiency with each hand was assessed by comparing the speed with which the child performs the peg-moving task with each hand. For this task, the child was presented with the apparatus with ten pegs in the holes further away from them. The presenter asked the participant which hand they preferred to use when writing (or drawing). Starting with the reported preferred hand, the presenter instructed the participant to move the pegs from the top row (further from the participant) to the bottom row (closer to the participant) one at a time, beginning with the peg closest to the hand being used. The participant continued to move the pegs sequentially from top to bottom until finishing with the peg on the opposite side of the apparatus. Two practice runs (one for each hand) were performed before data was collected to ensure that the participant understands the test procedure. After each trial, the apparatus was turned around, effectively resetting the test. If the child consistently interfered with the test procedure with their other hand, they were asked to place the hand not being tested behind their back. Once the participants performed the practice trials successfully, we tested each hand three times, starting with their reported preferred hand and alternating between hands with each successive trial. The time for each trial was measured to the nearest hundredth of a second using a digital stopwatch and recorded on a timesheet. The average times for each hand were then compiled, with the difference between these averages serving as a measure of differential performance.

It is important to point out that the infant and toddler portions of this study were previously performed and the results from these various assessments have already been published. (Nelson, Campbell & Michel, 2013; 2014; Michel, Babik, Sheu, & Campbell, 2013; Campbell, Marcinowski, Babik & Michel, 2015; Campbell, Marcinowski, Latta & Michel, 2015; Campbell, Marcinowski & Michel, 2018). The latent class assignments were sourced from this body of previous work as well. The 5-year assessments (both observation-based and proficiency-based) and all statistical analyses detailed here are original to this study.

4. Analyses

The primary focus of the study was to determine the ability of these early developmental forms of handedness to predict differential hand use preference and proficiency later in childhood. Six separate analyses were required to assess this predictive quality. The first three analyses examine the predictive relationships between the preferences observed at each time window: 6-14-month acquisition latent class predicting 18-24-month RDBM latent class, 6-14-month acquisition latent class predicting 5-year RDBM preference, and 18-24-month RDBM latent class predicting 5-year RDBM preference. The second three measure the predictive value of these preferences (6-14-month acquisition latent class, 18-24-month RDBM latent class, and 5-year RDBM preference) on hand performance differences at five years on the peg-moving task at 5 years.

Since unimanual and bimanual manipulations have already been shown to be at least partially related (Nelson, Campbell and Michel, 2013), I have used the portion of our resulting data that overlaps with theirs (our infant object acquisition data and toddler RDBM data) to attempt to perform a replication of their findings, using the McNemar-Bowker chi-square analysis to analyze the predictive value of latent class membership for acquisition across 6-14 months on latent class membership on RDBM at

18-24 months. While this replicative component is not the primary focus of the study, the consistency of these classifications represents a critical aspect of cascade theory that we have the opportunity to test.

If a group is divided into three classifications (in this case left, right, or no preference) at two different age levels, one expects a certain proportion of the group to be consistently classified by chance without any factors influencing this consistency. The McNemar-Bowker test of symmetry was chosen for this analysis to determine the consistency of classification in a 3x3 contingency table (special thanks to Peter Delaney and Doug Levine) and a one-way analysis of variance (ANOVA) was used to analyze the relationship between the observational measures and the peg moving performance differences. The McNemar-Bowker test was performed for left- and right-handers, as well as those not displaying a preference, for each of the three proposed predictive relationships (6-14-month acquisition latent class predicting 18-24-month RDBM latent class, 6-14-month acquisition latent class predicting 5 year RDBM preference, and 18-24-month latent class predicting 5 year RDBM preference) and an analysis of variance (ANOVA) was used for the relationships between each of these three behaviors and hand performance differences in a peg moving task at 5 years.

This study is an attempt to study hand preference development as a constructive process across age. The information provided by these analyses will help to create a more detailed understanding of the process of hand preference development as it progresses across childhood since this study pertains not only to the development of preference for individual behaviors, but the relationships that these preferences have to each other. This study also allows for the replication of previous findings, strengthening the literature on infant motor development.

CHAPTER III

RESULTS

1. Observational Measures

Of the 58 children for which we had data across all three time points, 24 (41.4%) displayed a consistent right-hand preference across all three time periods. Four (6.9%) children displayed a consistent left-hand preference across all three time periods. Only one (1.7%) displayed no preference across all three time periods. Ten more individuals (17.2%) exhibited no preference in infancy (6-14 months) but developed a preference in toddlerhood (18-24 months) that was again observed at 5 years. Eight (80%) of these developed a right preference in toddlerhood, and 2 (20%) developed a left preference.

Since there are three time periods being observed for hand preference consistency, there are three temporal comparisons to be made. The first comparison is the hand preference classification of the child in infancy (latent class across 6-14 months of age) with their classification in toddlerhood (latent class across 18-24 months of age). The second comparison is the classification in infancy with their classification at 5 years. Finally, the third comparison is the child's classification in toddlerhood with their classification at 5 years.

Table 1. Changes in Hand Preference Classification Across All Three Observational Comparisons. Letter code denotes consistency or shift in preference across comparison. L = Left, NP = No Preference, R = Right.

	Infant/Toddler	Infant/5	Toddler/5
R-R	26	26	33
R-NP	2	3	1
R-L	7	6	2
NP-R	8	9	5
NP-NP	2	1	2
NP-L	2	2	1
L-R	2	4	1
L-NP	4	1	2
L-L	5	6	11

Table 1 shows each comparison and how many children were in each development group. The letter combination on the left signifies the developmental change of each child. On the left side, the first letter (before the dash) represents the classification of the child at the first time point in the comparison and the second letter (after the dash) representing the hand preference classification at the second time point. "R" signifies a right preference or grouping into a right-preferential latent class, "NP" signifies no preference or grouping into a non-preferential latent class, and "L" signifies a left preference or grouping into a left-preferential latent class. Each column in **Table 1** represents a different comparison, with the first column of this figure representing the first comparison of hand preference in infancy with hand preference in toddlerhood, the second column representing the second comparison of hand preference in infancy with hand preference at five years, and the third column

representing the third comparison of hand preference in toddlerhood with hand preference at five years.

Figure 1, **Figure 2** and **Figure 3** graphically display the shifting classifications for each of the three temporal comparisons, along with charts that detail the numerical categorical shifts.

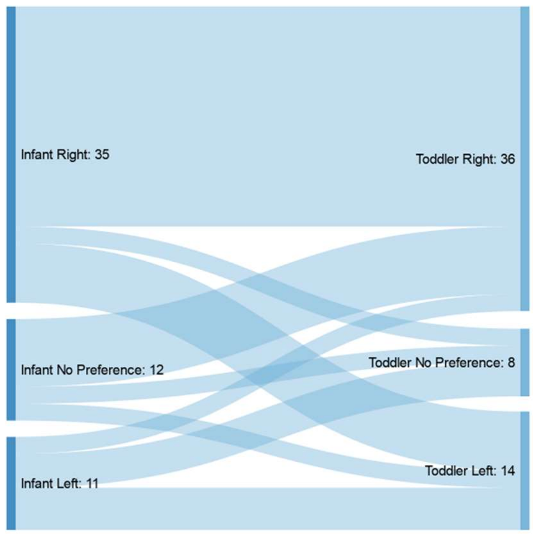
1.1. Comparison One: Infancy (6-14 Months) and Toddlerhood (18-24 Months)

Thirty-three (56.9%) of the 58 children in this comparison were consistent in their classifications from their first classification at 6-14 months to their classification at 18-24 months. Nine (15.5%) of the 58 were found to have switched hand preference classifications, with 7 (12.1%) switching from right-handed in infancy to left-handed in toddlerhood and 2 (3.4%) switching from left-handed in infancy to right-handed in toddlerhood. Ten (17.2%) children with no preference in infancy developed a preference in toddlerhood, 8 (80%) of these developing a right preference and 2 (20%) of them developing a left preference.

Twenty-six (44.8%) of the 58 children displayed a consistent right preference across both time periods. Two (3.4%) were classified as having a right preference in infancy, but in toddlerhood were classified as having no preference. Seven (12.1%) were classified as having a right preference in infancy but were classified as having a left preference in toddlerhood. Eight (13.8%) were classified as having no preference in infancy but were classified as having a right preference in toddlerhood. Two (3.4%)

were classified as having no preference in both infancy and toddlerhood. Two (3.4%) were classified as having no preference in infancy but were classified as having a left preference in toddlerhood. Two (3.4%) were classified as having a left preference in infancy but switched to a right preference in toddlerhood. Four (6.9%) were classified as having a left preference in infancy but classified as no preference in toddlerhood. Five (8.6%) displayed a consistent left preference across both infancy and toddlerhood.

A kappa analysis of this comparison showed significant agreement between acquisition hand preference latent class in infancy and RDBM preference latent class in toddlerhood (κ=.218, p=.023) with a confidence interval that did not include 0 (95% CI: .022 to .414) and 57% agreement between the two measures. In the McNemar-Bowker analysis of the relationship between latent class membership for acquisition across 6-14 months of age and latent class membership for RDBM across 18-24 months of age, it was found that there was no significant disagreement in assignment of handedness classification between the two measures (X^2 (3,58) = 7.044; p = .07). This means that as a group, the latent class (left, right, or no preference) that the infants were assigned to across 6-14 months did not differ significantly from the latent class that these same infants were assigned to in toddlerhood across 18-24 months.



Toddler RDBM Latent Class

Infant Acq. Latent Class	**Right**	**No Preference**	**Left**
Right	26	2	7
No Preference	8	2	2
Left	2	4	5

Figure 1. Categorical Shifts Between Infancy (6-14 Months) and Toddlerhood (18-24 Months)

1.2. Comparison Two: Infancy (6-14 Months) and RDBM Preference at 5 Years

Again, thirty-three (56.9%) of the children displayed a consistent preference between two time periods, and while the numbers are quite similar, there are some distinctions between this outcome and the previous comparison. One fewer child was classified as consistently no preference across this comparison than in the comparison of infancy and toddlerhood, and one more child was classified as consistently left-handed than in the previous comparison. While the numbers may be similar, this does not necessarily mean that the same children are represented in each classification group, although from the number of children that remain consistent across all three time periods, it can be concluded that many of them are. In this second comparison of hand preference in infancy and hand preference at five years, 26 (44.8%) of the children displayed a consistent right-hand preference in both infancy and at five years. Only one child (1.7%) was consistent in their classification as having no preference both in infancy and at five years. Six (10.3%) children were classified as consistently left-handed in both toddlerhood and at 5 years. Eleven (19%) children classified as having no preference in infancy displayed a lateralized preference at five years, with 9 (82%) developing a right preference and 2 (18%) developing a left preference.

Three (5.2%) children were classified as right-handed in infancy who were then classified as having no preference at 5 years. Six (10.3%) children were classified as having a right preference in infancy who were later classified as having a left preference. Four (6.8%) children were classified in infancy as having a left-hand preference who were later classified as having a right-hand preference. Finally, only one (1.7%) child was classified as having a left-hand preference in infancy but was classified as having no preference at five years. A kappa analysis of this comparison showed significant (though mild) agreement between acquisition hand preference latent class in infancy and RDBM preference classification at 5 years of age (κ=.188, p=.048). However, the 95% confidence interval for this estimate did include 0 (95% CI: -.018 to .394), and as in the first comparison, there was 57% agreement between the measures. In the McNemar-Bowker analysis of the relationship between latent class membership for acquisition across 6-14 months of age and preference classification for RDBM at five years of age, it was found that there was no significant disagreement in assignment of handedness classification between the two measures ($\mathbf{X}^2$ (3,58) = 3.733; p = .292). This means that as a group, the latent class (left, right, or no preference) that the infants were assigned to across 6-14 months did not differ significantly from the hand preference group these same children were classified into at five years.

Infant Acq. Latent Class	*Five-Year-Old RDBM Classification* Right	No Preference	Left
Right	26	3	6
No Preference	9	1	2
Left	4	1	6

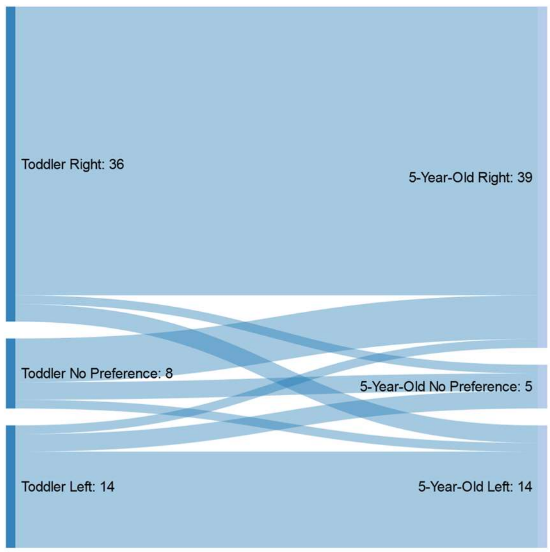
Figure 2. Categorical Shifts Between Infancy (6-14 Months) and Five Years

1.3. Comparison Three: Toddlerhood (18-24 Months) and RDBM Preference at 5 Years

Compared to the first two comparisons, many more children displayed a consistent hand preference across this time period. Forty-six (79.3%) of the 58 children retained the hand preference category that had been classified across their assessments during toddlerhood. Thirty-three (56.9%) were consistently right-handed and 2 (3.4%) were consistently classified as having no preference. Perhaps most importantly, eleven (19%) of the children were consistently classified as left-handed. Six additional children (10.3%) classified as having no preference in toddlerhood developed a preference by 5 years, with 5 (8.6%) of those developing a right preference and 1 (1.7%) developing a left preference.

Given the much greater proportion of the sample that falls into the consistent category, the number of children with an inconsistent classification naturally falls. A total of six (10.3%) children fell into these categories. One (1.7%) child that was classified as right-handed in toddlerhood was classified as having no preference at five years. Two (3.4%) children that displayed a right preference in toddlerhood switched to displaying a left preference at five years. One (1.7%) child made the switch in the opposite direction, displaying a left preference across toddlerhood, but a right preference at five years. Finally, two (3.4%) displayed a left preference in toddlerhood and later displayed no preference at five years.

A kappa analysis of this comparison showed significant agreement between toddler RDBM latent class and RDBM preference classification at five years of age (κ=.596, p<.001) with a confidence interval that did not include 0 (95% CI: .022 to .414) and 79% agreement between the two measures. In the McNemar-Bowker analysis of the relationship between latent class membership for RDBM across 18-24 months of age and hand preference classification for RDBM at five years of age, it was found that there was no significant disagreement in assignment of handedness classification between the two measures ($\mathbf{X}^2$ (3,58) = 3.333 ; p = .343). This means that as a group, the latent class that the toddlers were assigned to (right, left, or no preference) across 18-24 months did not differ significantly from the hand preference that the children displayed at five years.



Toddler RDBM Latent Class	Five-Year-Old RDBM Classification: Right	No Preference	Left
Right	33	1	2
No Preference	5	2	1
Left	1	2	11

Figure 3. Categorical Shifts Between Toddlerhood (18-24 Months) and Five Years

2. Proficiency Measures

The peg-moving tests were administered at five years of age and were compared to the results from each of the observational measures of hand preference (latent class across infancy, latent class across toddlerhood, and RDBM preference at five years.) For these 43 children, the mean hand speed difference score was 1.05 (s = 2.49), meaning that the group was, on average, just over a second faster with their right hands to move the ten pegs from the top row to the bottom row across their three trials. There was considerable variability in the scores, which ranged from -6.57 to 5.88.

Figure 4 shows a histogram of the distribution of frequencies of the hand speed differences at five years observed in our sample.

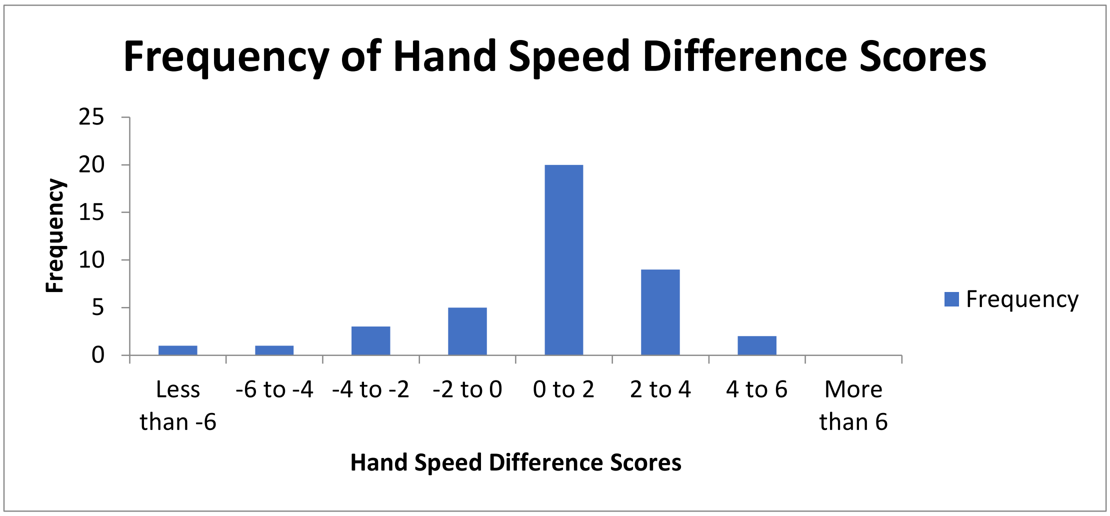


Figure 4. Frequency Distribution of Hand Speed Difference Scores for Peg-Moving Task

2.1. Comparison One: Infant Acquisition Latent Class and Peg-Moving at Five Years

In the first comparison, the children classified as right-handed in infancy were on average nearly 2 seconds (1.999 seconds) faster at five years in the peg-moving task with their right hands than they were with their left, showing a considerable proficiency gap between their hands. The children that with no hand preference in infancy were nearly a second (0.855 seconds) faster with their right hand than they were with their left, suggesting that many of the individuals in this group, while not displaying a preference in infancy, may end up classified as right-handed as they develop. Finally, the group of children classified as left-handed in infancy were nearly a half-second

(0.499 seconds) faster with their left hands than with their right. This shows that even across the ages of 6-14 months, these children were developing a preference that they would carry forward across their childhood.

The omnibus ANOVA test suggests a significant difference in hand speed difference scores between the infant groups (F (2, 41) = 3.805; p=.031). When further analyzed with a post-hoc Tukey's HSD, the group of children that displayed a right-hand preference in infancy were significantly different in their hand speed difference scores from those children who displayed a left-hand preference (p=.025). However, the analysis showed that neither the infant right-handed group nor the infant left-hand group showed a significant difference in hand speed difference scores from those that displayed no hand preference in infancy (p=.363 when compared with left-handers, p=.372 when compared with right-handers).

2.2. Comparison Two: Toddler RDBM Latent Class and Peg-Moving at Five Years

In this comparison, we analyzed the five-year hand speed difference scores of the toddler RDBM hand preference latent classes. On average, the left-handed latent class (n=15) was slightly faster with their left hands than with their right (0.579 seconds). The no-preference latent class (n=10) was roughly a second faster with their right hands than with their left (1.114 seconds), and the right-handed latent class (n=18) was much faster with their right hands than with their left. (2.371 seconds).

The differences in the hand speed difference scores between the five-year RDBM groups were then analyzed, also using a one-way ANOVA. The omnibus test was significant ($F(2,42) = 8.148$; $p=.001$), signifying a significant difference in hand speed difference scores among the three latent classes. As in the previous comparison, this prompted further analysis with a Tukey's HSD. This revealed that the hand speed difference scores of the left and right latent classes were significantly different from each other at five years ($p=.001$), but as in the infant comparison, the no preference latent class was not significantly different from either the right ($p=.291$) or the left ($p=.130$) latent classes.

<u>2.3. Comparison Three: Five-Year RDBM Preference and Peg-Moving at Five Years</u>

Next, the five-year hand speed difference scores of the preference groups for RDBM at five years were analyzed. On average, the left-handed RDBM group (n=13) showed nearly no difference in hand speed in the peg-moving task (0.005 seconds faster with right hand). Interestingly, the no-preference RDBM group (n=6) was slightly faster on average with their left hands than their right hands at five years (0.358 seconds), showing more of a preference for the left hand than even the left-handed group. Finally, the right-handed RDBM group(n=36) was on average much faster (2.014 seconds) faster on average with their right hands than their left hands.

This comparison was also analyzed using a one-way ANOVA. As in the first two comparisons, the omnibus ANOVA test showed that there were significant differences in hand speed difference scores across the three groups (F(2, 54)=4.625; p=.014). The follow-up Tukey's HSD showed that as in Comparison 2, the hand speed difference scores driving this significant result were those between the left and right preference groups. These were significantly different from each other (p=.04), but as in the previous comparison, the no preference group was not significantly different from either the left (p=.952) or the right (p=.085) preference groups. The inability to find a difference between the two groups displaying a preference and the no preference group is likely driven by the diminishing sample size of the no preference group as the children increasingly display hand preferences across development.

CHAPTER IV

DISCUSSION

The goal of this study was to determine the predictive value of measures of early hand preference, and the results strongly suggest that both the infant and toddler measures are reliable in their prediction of hand preference at five years. These results are consistent across all three comparisons, meaning that even in infancy, hand preference can be stable enough to be consistent across development into toddlerhood and later childhood. Also, in infancy, the population-level bias toward right-handedness that is so evident in the adult general population is clearly seen in our sample at each assessment. A majority of the infants in the sample display individual-level lateralization bias, and the proportion of children that display an individual preference increases at every time point, with the no preference groups shrinking from 31.0% of the sample in the 6-14 month assessments, to 23.3% of the sample in the 18-24 month assessments, to a mere 10.9% not displaying an RDBM preference at five years. The portion of our study that offered the opportunity to replicate previous findings (Comparison 1 of the observational section) found similar results to what the previous study (Nelson, Campbell and Michel, 2013) found. The present study found that infant acquisition latent class does not differ significantly in its classification of children from toddler RDBM latent class, supporting the earlier study's findings and strengthening the case for the cascade of preference for one skill into preference for a more complex skill that develops later.

The results of the observational comparisons supported three predictions concerning the predictive quality of early hand preference development. Comparison One showed that infant acquisition hand preference was predictive of toddler RDBM hand preference. Comparison Two demonstrated that infant acquisition hand preference was predictive of RDBM hand preference at five years. Finally, Comparison Three showed that toddler RDBM hand preference was predictive of RDBM preference at five years. Given the consistent nature of the manual bias seen across the development of the children in our study, it becomes evident that the development of hand preference is not a milestone that is achieved once a certain level of biological maturity has been reached and is instead a bias that begins early in development with simple manual actions that cascades into a stable, predictable preference for more complex behaviors.

In the peg-moving comparisons, significant differences were seen between the left- and right-handed groups when analyzed from any age group. This means that the predictive quality of early hand preference that was found in the observational tasks holds true for measures of proficiency as well. However, this measure is not completely reliable, as even at the same visit in which the children were assessed for RDBM preference at five years, there was considerable variability in the differences in hand speed scores in the children that showed a significant preference.

Considering the previous studies that examined the developmental trajectories of these manual skills provides interesting opportunities for future studies. In examining the developmental trajectories of object acquisition, Campbell and colleagues (2018) found four latent classes that defined the development of this manual action across the 6-14 month time window. These trajectories showed considerable change across the developmental window, indicating a period of active development. However, when RDBM was assessed in these same children across the 18-24 month time period, the four distinguishable latent classes showed flat trajectories (slopes were not significantly different from 0). This suggests that some stabilization of preference has occurred across the 14-18 month window, but there is insufficient data to either support or disprove this hypothesis. It seems that this specific age window would be particularly informative if included in a future longitudinal study. Given that the results of this study show such strong support for the cascade theory, this suggests that more complex behaviors develop later in childhood will follow the same pattern shown here and be predicted by early hand preference development.

This study also has other implications outside those directly associated with hand preference. If hand preference is stable as early as infancy, then this also suggests that the lateralization of other functions associated with the lateralization of hand use such as language is stabilizing across this age range, as well. Also, if Annett's theory of psychopathology and lateralization is true, then this suggests that the neurological changes associated with developing handedness may be occurring across the same developmental window as those associated with psychopathologies, and that these changes may become evident around this age range as well.

This study does have a few limitations. First, the size of the longitudinal (infant to five year) sample was only 58 individuals, which is greatly reduced from the numbers seen in the infant portion of the study. This limits the generalizability of the findings and makes distinction of differences between groups difficult. Perhaps with a larger sample, the differences in the hand speed difference scores would have provided more robust results. This is also the reason that an ANOVA analysis was not done looking at only the children who were consistent across development. The sample size would have been much smaller than the test that was already run, and the "No Preference" group would consist of only one individual. Also, the sample of 58 children were much less ethnically diverse than the population from which the sample was drawn. How this would have changed the results is unclear, but it is difficult to make definitive statements about a population with a sample that does not resemble the population from which it was drawn.

What cannot be concluded from the results of the current study is the definitive nature of the origin of hand preference. While this study does help to elucidate aspects of the nature of its development, no conclusion can be drawn from this design as to its origin. This design would display the same outcome if handedness had a single-allele genetic origin as it would if handedness had a postural developmental origin. This is not to say that the nature of this origin cannot be ascertained, but simply that this design does not touch on development early enough to explore it. Nor does this study deeply examine the development of each individual manual action across this developmental period. A nearly exhaustive analysis of RDBM development has already been written (Babik and Michel, 2016a, b, c), and other individual actions have been examined at length. The resilience of hand preference to outside influences is also not a factor in this study, although the concept does provide fodder for future studies. The handedness of the parents is also not included in the analyses, though there has been some data gathered that could be analyzed in the future.

Overall, this study adds important features to a picture of hand preference development that is starting to become clearer as the literature accumulates. It emphasizes the importance of the development across the first year and the stability of the lateral biases that are formed during this period, as these biases can predict development from this point onward. This study also highlights other differences that can be predicted by the preferences developed across infancy and, while the peg-moving measure may not have provided as much clarity as was originally hoped for, it also provided a comparison of different methods of assessing hand preference in children. It also provides a promising base upon which to build other studies of consistency looking at later development since it has now been shown that there is consistency across infancy, toddlerhood, and later childhood.

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APPENDIX A

LABORATORY FIGURES

Figure 5. Peg-moving Apparatus with Pegs Removed. This shows the peg-moving apparatus used to test the hand proficiency of the five-year-old group. Two of the pegs have been removed.

Figure 6. Presentation Setup and Table. This is the semi-circular table used for toy presentations. The child (with or without their parent) sits in the blue chair in the middle with the presenter seated directly across from them.