Differential persistence of Primary Reflexes for Children with Autism Spectrum Disorder: A systematic replication

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Short title: Primary Reflexes and ASD.

Journal of Autism and Developmental Disorders.

Abstract

Primary reflexes are highly stereotypical, automatic movements comprising much of the motor repertoire of newborns. The current study examined rates of presence of five primary reflexes (snout, visual rooting, sucking, tactile rooting, and grasp) for children with ASD (*n*=35), developmental disability (*n*=30), and typically developing children matched to participants with ASD on chronological age (*n*=30), and variables predictive of their persistence. There was a higher prevalence of snout, and visual rooting, reflex among children with ASD. These data suggest that the persistence of primary reflexes holds promise as a biomarker for autism spectrum disorder (ASD)

Keywords: autism spectrum disorder, primary reflexes, snout reflex, visual rooting reflex, sucking reflex, tactile rooting reflex, grasp reflex

The identification and diagnosis of ASD is a topic of intense study and investigation (Ozonoff et al., 2009). Symptoms of ASD are present for a significant amount of time before a formal diagnosis is received (Lauritsen, 2013), and parents report identifying features of ASD in their children as early as 12 months of age (Matson, Wilkins & Gonzalez, 2008; Ozonoff et al., 2009). However, average age of diagnosis is 5.7 years (Shattuck et al., 2009), and a significant minority of children with ASD are likely to be undiagnosed (Yeargin-Allsopp et al., 2003). Substantial research highlights the importance of early diagnosis and intervention, and more positive prognosis for individuals and their families (Zachor & Curatolo, 2014; Dawson et al., 2012). In light of this discrepancy between the importance of early diagnosis and difficulty with prompt diagnoses, research attempted to bridge the temporal gap between initial parental concerns and formal diagnosis (Johnson & Meyers, 2007).

In order to identify individuals with ASD, and initiate interventions, at the earliest possible age, research has explored potential precursors or biomarkers for ASD (Matson, Wilkins & Gonzalez, 2008; Zaman et al., 2016). While not currently incorporated in clinical diagnostic practice (Loth et al., 2016), a number of biomarkers have been recently proposed (Goldani et al., 2014). Developmental biomarkers are a type of biomarker for ASD that has been examined in recent years. As the central nervous system matures, spontaneous, involuntary movements are suppressed and replaced with more functional, goal directed movements (Torres, 2013). One specific class of involuntary movements, known as Primary Reflexes (PR), has been suggested to be atypical among persons with ASD. According to Zafeirou (2004), PR are brainstem mediated, automatic responses crucial to survival in the early months of life. PR occur as early as gestational week 25-26, and comprise one of the earliest, simplest, and most frequently used tools among child neurologists to assess the integrity of the central nervous system of infants (Bilbilaj, Gjipali & Shkurti, 2017; Menkes

et al., 2006). In typical development, PR are usually inhibited completely by the end of the first year pospartum. There is a growing body of evidence to suggest that the persistence of PR beyond the early months of life may be related to malfunctions in cerebral cortex inhibition and the subsequent diagnosis of neurodevelopmental disorders such as ASD (Hobo et al., 2014; Minderaa et al., 1985).

PRs commonly examined in early neurological assessments include the snout reflex, the visual rooting reflex, the sucking reflex, the tactile rooting, and the grasp reflex (Minderaa et al., 1985; Walker, 1990). Minderaa et al. (1985) investigated the presence of PRs in individuals with ASD and typically developing (TD) controls. There was a significantly higher prevalence of the snout reflex and the visual rooting reflex in the ASD group compared to TD controls. de Bildt et al. (2012) investigated the presence of the visual rooting reflex in individuals with ASD, and found it elicited in individuals with ASD more often than those with intellectual disability, and pervasive developmental disorder not otherwise specified. These two studies have yielded data suggestive of a relationship between the presence of PR beyond infancy and a diagnosis of ASD and indicate the potential diagnostic value of PR within ASD.

The current study aimed to systematically replicate the above two studies, and to examine the presence or absence of PRs in children with ASD, developmental disability (DD), and a chronological age-matched group of typically developing children. By including the additional comparison group of Developmental Delay and directly comparing these three groups of children, it provides a new analysis of delineating potential differences in sustained PR. PR were consistently found to be significantly more prevalent in individuals with ASD, then testing for the presence of those reflexes after they are typically believed to recede could potentially become a simple precursor assessment for the detection of ASD within the first year of an infant’s life (Reed, 2007).

Method

Participants

Participants were recruited from mainstream schools, or special schools catering to children with a range of additional learning needs, in the Republic of Ireland. The children had to be aged between 4 and 6 years old, with a diagnosis made by a clinical psychologist independent of this study using DSM criteria and clinical judgment, of Autism Spectrum Disorder (ASD), a Developmental Delay (DD), or be typically developing (TD). There were no other inclusion or exclusion criteria. Ethical approval for this research study was granted by the School of Psychology Research Ethics Committee.

Ninety-five children, between the age of 4 to 6 years, participated. There were 35 children diagnosed with ASD, 30 with Developmental Delay, and 34 Typically Developing children matched with the ASD group on chronological age. The ages, genders, and clinical history of the participants is shown in Table 1.

Table 1 about here

Materials

Primary Reflex: The measured PRs were the: snout, visual rooting, sucking, tactile rooting, and grasp, by a researcher with training in appropriate assessment of PRs. Each PR was measured twice. If after the second measure the response was deemed ambiguous, that PR was re-tested until a definite response was determined (de Bildt et al., 2012; Walker, 1990).

Snout reflex was tested by a soft rubber reflex hammer, or by exerting firm pressure with the index finger, beneath the nose on the upper lip. Contraction of the muscles causes

the mouth to resemble a snout (Walker, 1990). The snout was scored present if puckering, pouting, or contractions of the muscles at the base of the nose, occurred.

Visual rooting reflex was assessed by slowly approaching the child's visual field with the reflex hammer. The visual rooting reflex was scored present for any forward movement of the head in the direction of the reflex hammer (as if to touch it), and protrusion or opening of the mouth occurred.

Sucking reflex was assessed by gently stroking the medial area of the upper and lower lip with the index finger, and approaching the lips with an object (Walker, 1990). The sucking reflex was scored present if the lips closed around the finger, or licking movements were observed.

Tactile rooting reflex was assessed by stroking the corners of the mouth and by stroking the right and left cheek. The tactile rooting reflex was scored present, if any turning the head or mouth toward the reflex hammer, with or without sucking movements, occurred.

Grasp reflex was assessed by stroking the palm of the child's hands with the head of the soft rubber reflex hammer. The grasp reflex was scored present if any flexion of the fingers occurred. During positive responses, the fingers will curve, much like a bird's claw, and grip the stimulus.

Procedure

Sessions with each participant lasted approximately 15-30 minutes, and were conducted individually in the participant's school environment. Habituation to the reflex hammer allowed participants to observe the reflex hammer, touch the reflex hammer, and see the researcher model what the reflex hammer would be used for (e.g., the reflex hammer was lightly tapped beneath the researcher's nose). No time limit was placed on the habituation process. Habituation was indicated when the participant did not show any indication of

distress (e.g., pushing away, grimacing, refusing to have the reflex near them, or any vocal indications of distress. If a participant indicated distress, the PR being measured was terminated.

When habituation was complete, the researcher began implementing the reflex measures. During PR measurement, a second observer rated participants to assess agreement. If the raters disagreed on the response exhibited, the reflex was examined again until consensus was achieved. Cohen's κ assessed level of agreement between the two raters, and found excellent inter-rater agreement: snout reflex (κ = 1.00), sucking reflex (κ =.821), tactile rooting reflex (κ =.938), visual rooting reflex (κ =1.00), and grasp reflex (κ =.883).

Results

Based on the data shown in Table 1, chi square analysis revealed no statistical difference between the genders in the groups, $X^2(2) = 5.452$, $p = .065$, $\varphi = .240$. Analysis of variance (ANOVA) indicated no significant difference between the ages of the groups, $F(2,92) = 2.85$, $p = .064$, $\eta^2_p = .058$[*95% CI* = .000:.157].

Table 1 about here

Table 1 presents the frequency of each of the five primary reflexes for each group. Inspection of these data shows greater persistence of primary reflexes for ASD ad DD groups compared with the TD group. The ASD group also had higher levels of persistence compared to the DD group. There were significant associations (using a Bonferroni correction: p = .05/5 = .01) between group and presence of: snout reflex, $X^2(2) = 16.674$, $p < .001$, $\varphi = .419$; visual rooting reflex, $X^2(6) = 14.828$, $p < .001$, $\varphi = .395$; but not with the sucking reflex, $X^2(2) = 3.575$, $p = .167$, $\varphi = .194$; tactile rooting reflex, $X^2(2) = 3.031$, $p =$

.220, φ = .179; or grasp reflex, X^2 (2) = 4.541, p = .103, φ = .103. For the analysis that were significant, portioning of the table to allow comparison between ASDD and non-ASD participants, showed a significant difference for the snout reflex, X^2 (1) = 12.085, p < .001, φ = .357; and for the visual root reflex, X^2 (1) = 8.834, p = .005, φ = .305.

A discriminant function analysis conducted to analyse if the persistence of PRs differentiated the three groups, and found the first function significantly differentiated the groups, *Wilks Lambda* = .687, X^2(10) = 33.853, p < .001, φ = .597. According to the structure matrix, the first function included persistence of visual rooting (.712), snout (.667), and to a lesser extent sucking (.326) reflexes. Examination of the functions at the group centroids revealed that the ASD group had strong positive association with the factor (.592), the DD group had weak positive association (.140), and TD group had strong negative association (-.830). The function predicted group membership with 58% accuracy.

Figure 1 about here

A series of ROC analyses were performed to determine the degree to which the presence of the reflexes could predict the presence of ASD versus its absence (i.e. comparing those with ASD with those in the two groups without ASD). The presence of any one of the three implicated reflexes (visual rooting, snout, and sucking) on its own gave only a small area under the curve: visual rooting = .63 (.51:.75); snout = .66 (.54:.78); sucking = .54 (.42:.66). Using the two stronger reflex predictors (visual rooting and snout, thus giving a value of 0 to 2 in terms of reflexes present) the area under the curve was .72 (.60:.83). The addition of the third reflex (sucking; giving a possible reflex score of 0 to 3), produced an area under the curve of .73. (.61:.84; standard error = .056). Analysis of the three-reflex model (shown in Figure 1) shows that the area under the curve was significantly greater than

that which would be expected by chance, $p < .001$. For the presence of one reflex (of any sort) the sensitivity was 91% and the specificity was 77%; for the presence of two reflexes the sensitivity was 100% and specificity 94%.

Discussion

A small body of research has suggested that the persistence of primary reflexes past early infancy is a potential precursor for ASD. The current results indicated that the snout and visual rooting reflexes presented with higher frequency for the ASD group in comparison with DD and TD children. This finding is consistent with those reported by de Bildt et al. (2012) and Minderaa et al. (1985). Specific characteristics associated with ASD may explain the difference found between the ASD and DD group. For example, one symptom domain of ASD includes restricted interests and repetitive behaviors that has been previously described as a potential threshold for the presence of one type of PR- the visual rooting reflex (de Bildt et al., 2012). The negative results yielded in this study in relation to the sucking reflex, the tactile rooting reflex and the grasp reflex also are similar to those reported by Minderaa et al. (1985). This replication of higher prevalence of specific persisting reflexes among persons with ASD suggests these could be considered a biomarker.

It has been suggested that sustained PR beyond six months of age may indicate neurological alteration in functioning at the cortical and subcortical areas of the brain and maturational delay in the nervous system that is associated with inhibition of these reflexes (Duchan, 2021). Furthermore, it could indicate abnormal asymmetrical development of the brain hemispheres (Sigafoos, Roche, O'Reilly, Lancioni, 2021). Identifying such alteration and delay could be useful given the heterogenous nature of the condition and the delays associated with diagnosis. According to de Bildt and colleagues (2005) elicitation of PR after infancy may indicate reduced inhibition of brainstem reflexes. Sustained PR could delay the

maturational processes in the brain that ultimately inhibit these reflexes. Therefore, PR differences in autistic children may provide an important means of examining the neurological alterations associated with ASD. ASD is a highly heterogenous condition and providing ways of delineating differences in such neurological alterations may provide an effective and efficient means of dissecting such heterogeneity (Minshew, Sweeney, Bauman, & Webb, 2005).

As PR are a developmental phenomenon, it may be predicted that younger children with ASD sustain PR. However, comparing prevalence rates across the three studies does not support this view. The eldest sample of persons with ASD (Minderaa et al., 1985) exhibited the highest frequency of positive responses to the visual rooting reflex, suggesting that PRs may subside in the early years of a child's life, and reappear later in life. Future research could potentially examine the reappearance of the VRR at a later stage in a child's life, or if a child who fails to repress PRs after six months is likely to retain that reflex for the remainder of their life.

Future research could consider the potential benefits of examining the differences in PR presentation between subtypes of ASD. This would broaden the knowledge on the behavioural and developmental characteristics that are specific to different types of ASD. The current study did not identify predictors of sustained PR, and it would be useful in future research to examine variables such as challenging behaviour and social skills to help us better understand the relationship between ASD and PR. Finally, the exploration of other types of PR that have not yet been associated with ASD would be beneficial in future ASD biomarker research. Other PR that could be examined include the galant reflex, the moro reflex, the plantar reflex, the babkin reflex and the parachute reflex. The retention of these reflexes past a certain age are said to indicate pathology (Schott & Rossor, 2003), however, they are yet to be investigated in a sample of persons with ASD.

The identification of early behavioral signs that are predictive of ASD made during routinely administered assessments would bring forward by 6-12 months detection of a child at risk of ASD, perhaps allowing detection in the first year of life. The clinical utility of such a measure may contribute to autism risk assessment. Many existing diagnostic indicators need to be administered later in the infant's development, other potential predictors of ASD-related problems that can be checked earlier (such as testosterone levels from amniocentesis procedures) require expensive technology or are not routinely administered at all. Thus, if persistent PRs could be established as a correlate of ASD it would represent a significant practical and temporal advance in the early detection of ASD.

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Table 1: Participant characteristics.

	Autism Spectrum Disorder	Developmental Delay	Typically Developing
N	35	30	30
Gender (male)	30	19	25
Age (standard deviation)	4.6 (1.75)	5.20 (.63)	5.20 (0.55)
Diagnosis	29 (83%) ASD 1 (3%) PDD-NOS 1 (3%) ASD + ID 4 (11%) ASD + other	12 (40%) ID only 8 (27%) Down's 3 (10%) Genetic disorder 7 (23) Other developmental disorder	
Medication	11 (32%) None 8 (23%) Melatonin, Movicol 46% No information	14 (46%) None 7 (23% Melatonin, Movicol 5 (16%) More than two 3 (10%) No information	
Other health conditions	8 (23%) None 2 (6%) Asthma 1 (3%) Pica 1 (3%) Hirschsprung's Disease 1 (3%) Febrile convulsions 19 (54%) No information	20 (67%) None 4 (13%) Asthma 4 (13%) Febrile convulsions 1 (3%) Sensory processing disorder 11 (37%) No information	

Table 2: Prevalence of the Five Primary Reflexes across the Four Groups.

Group	Snout	Visual rooting	Sucking	Tactile rooting	Grasp
Autism Spectrum Disorder	15 (43%)	14 (40%)	4 (11%)	2 (6%)	2 (6%)
Developmental Delay	7 (23%)	8 (26%)	2 (6%)	3 (10%)	4 (13%)
Typically Developing	0	0	0	0	0

Figure 1: ROC analysis for the presence of visual rooting, snout, sucking reflex in predicting ASD.