



OPEN Manual and automated assessments of general movements in neonates are associated with early autism risk at 18 months

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General movements (GMs) refer to infants' spontaneous motor activities before the emergence of voluntary motor activity. Abnormal GMs in neonates have been regarded as a marker of poor neurodevelopmental outcomes, with preliminary findings in autism. To examine the relation between abnormal GMs in neonates and autism risk, videos of neonates ($n = 76$) extracted from a Japanese birth cohort were retrospectively exploited. A manual assessment of GMs was completed using the General Movement Assessment Optimality Score (GMOS-R) rated by professionals blinded from all clinical information. An automated assessment of several features of neonates' motor activity was also conducted using videos of neonates. Outcome measures were the M-CHAT score at 18 months to document autistic risk status and the Strengths and Difficulties Questionnaire (SDQ) at four years to measure non-autistic general psychopathology. The GMOS-R total score and subscores significantly predicted the autistic risk status according to M-CHAT, but not any SDQ scales or the Total Difficulties score. In the manual assessment of GM, "Global poorness of motion" was the most informative feature in predicting ASD risk. The classification performance systematically increased with the addition of automatically extracted features, as indicated by the Loglikelihood tests. In contrast, the DeLong tests for comparison of AUC failed to reach statistical significance. Such improvement came mainly from incorporating information about the imbalance in motion strength between the upper and lower limbs, and was more marked for awake babies. This finding confirms the relevance of considering abnormal motor patterns in neonates as an early marker of autistic risk.

Keywords Motor development, Infants, Neurodevelopment, Early detection, ASD, General movement assessment

Abbreviations

AF	Automatic features
AOSI	Autism observation scale for infants
ASD	Autism spectrum disorder
AUC	Area under the curve
C-MACH	Chiba study of mother and child health
GMs	General movements
GMA	General movement assessment
GMOS	General movement assessment optimality score
GMOS-R	General movement assessment optimality score – revised form
ITC	Infant toddler checklist
M-CHAT	Modified checklist for autism in toddlers
NDD	Neurodevelopmental disorder
PCA	Principal component analysis
SDQ	Strengths & difficulties questionnaire

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General background

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder (NDD) underpinned by complex genetic and environmental risk factors. The diagnosis of ASD requires the association of impairments in several domains, including communication, reciprocal social interactions, stereotypical behaviors, and sensory particularities¹. The importance of early identification of infants at risk of ASD is to provide intensive intervention to offer the best neurodevelopmental outcomes². Whitehouse, Varcin³ showed that a program starting in infants identified as at-risk for ASD at 12 months significantly reduced ASD symptom severity at 3 years, and then the odds of an ASD diagnosis, compared to treatment as usual.

The standardized screening tools for ASD in the literature provide an overall estimation of ASD risk; however, their predictive performance remains limited⁴. Furthermore, several studies have aimed to detect ASD risk at even earlier stages, within the first year or even the initial months of life. For instance, the Infant Toddler Checklist (ITC) has been shown to assess ASD risk from as early as nine months of age⁵, while the Autism Observation Scale for Infants (AOSI) has attempted detection as early as six months⁶. The PREAUT grid identifies risk even earlier, with half of the positive screenings at four months associated with the onset of NDDs⁷.

Motor impairments in infants at high risk of ASD

While atypical motor patterns are not included among the diagnostic criteria for ASD¹, cumulative evidence in the literature converges on the observation of atypical motor patterns in infants at high familial risk of developing ASD^{8,9}. In addition, there is growing recognition of altered motor development in neonates who ultimately develop an ASD or other NDDs^{10,11}.

Altered motor development could precede the observation of abnormal communication, which is usually noticeable only after the first year^{2,12–14}. Besides, early infant motor skills are regarded as a key prerequisite for emerging social and communication abilities in typical^{15,16} and at-risk infants¹⁷. For example, infants' early spatial-motor skills are thought to provide a basis for the body's organization, which ultimately supports the emergence of communication skills. Infants who struggle to stabilize their head in the midline might find it more challenging to maintain a gaze fixation involved in the interpretation of adult facial expressions. Indeed, infants who later received a diagnosis of ASD at the age of 3 were more likely to show a head lag during the Pull To Sit test¹⁸. Other authors have noted the persistence of primitive reflexes in babies later diagnosed with ASD¹⁹.

General movements

Prechtl coined the notion of General movements (GMs) in the early 60s to describe infants' spontaneous motor activities before the emergence of voluntary motor activity. Three types of GMs are differentiated and show a developmental timeline: intrauterine and preterm movement (before childbirth), writhing movements (from birth to the 8th week), and fidgety movements (from the 9th week to 20 weeks)^{20,21}. Writhing movements are traditionally described as large contortions of the baby's entire body. Then, around the 8th to 9th week of age, the movements move closer to the body axis and reduce amplitude to take on a so-called fidgety feature. GMs were initially used to detect the risk of cerebral palsy^{20,22} in infants with acute medical conditions. This assessment has also been shown to be valid in predicting neurological outcomes in infants with genetic syndromes^{23,24} and in those born preterm^{25,26}.

Einspieler et al. developed the General Movement Assessment Optimality Score (GMOS), a measuring tool of GMs in neonates during preterm and term periods²⁷. The same team showed a good predictive performance of the GMOS-R, a modified version of the GMOS, for predicting neurological outcomes in babies born with a medical condition²⁸. To date, the GMOS-R has not been used to document GMs in a study on autism risk.

GMs and ASD

To the best of our knowledge, only three studies have specifically examined the features of GMs in infants at risk of ASD^{29–31}.

Phagava, Muratori³⁰ have retrospectively analyzed the home videos provided by parents of 20 children later diagnosed with ASD and 20 healthy controls matched for age. Videos were made in infants aged 0–2 months or 3–5 months, and two independent observers conducted global and detailed assessments of GMs. During the

writhing movement period, 70% of sequences of a group of infants later diagnosed with ASD showed a poor repertoire of GMs versus 13% of the sequences in the control group.

Einspieler, Sigafos²⁹ reviewed all case reports and series reporting GMs in infants with ASD. In addition to the cases previously published by Phagava, Muratori³⁰, the authors found five other cases of individuals with ASD and 17 babies with Rett syndrome, a genetic neurodevelopmental condition associated with severe communication and social interaction deficits: 17 out of 25 individuals with ASD (68%), and 100% of individuals with Rett syndrome presented abnormal GMs.

Zappella, Einspieler³¹ examined home videos retrospectively collected from parents of 18 children who presented autistic behavior at age two, with 10 of them finally being diagnosed with ASD. Three videos were analyzed for each participant during the first six months (1–2 months, 3–4 months, and 6 months). Three professionals rated age-specific movements, including swiping and wiggling (oscillating arm movements), kicking, movements towards the midline, and antigravity movements. They also assessed GMs specifically for each period (writhing or fidgety). Nine out of 10 infants later diagnosed with ASD presented abnormal GMs (fidgety), and 7/8 young who did not develop ASD had normal GMs. Interestingly, all parents reported that their child's development was normal before one year of age, and abnormal socio-communication signs (smile response, eye contact) did not discriminate between those with or without a final diagnosis of ASD.

More recently, some research has been conducted to determine how automated video feature extraction of infants' spontaneous motor activities could inform their risk of developing ASD^{32–34}. Caruso, Gila³² used the automated MOVIDEA software to compare the motor patterns of infants in a group of low-risk siblings of typical children ($n = 53$) and a group of high-risk ASD siblings ($n = 50$). Videos were collected for each participant five times between childbirth and 24 weeks, with a clinical assessment at 36 months. These authors concluded that high-risk infants had increased general motor activity associated with reduced variability and speed and increased acceleration of overall movement in space. Additionally, they observed an increase in limb movements, particularly of the upper limbs, during the first 12 weeks of life. This is consistent with the difficulties observed in autistic children regarding difficulties in postural control and goal-directed movements^{35,36}.

Doi, Iijima³³ used an automated procedure to analyze videos made with a more standardized procedure (in a laboratory) at 4 months among 18-month-old infants, ultimately classified in a high- vs. low autistic risk status (respectively, $n = 34$, $n = 17$) based on the Modified Checklist for Autism in Toddlers (M-CHAT) parental questionnaire. All classification models tested were regarded as having good properties on the sample, with a sensitivity of 0.71 and a specificity ranging from 0.88 to 0.97. The critical motor features discriminating between the two groups were a decrease in the frequency and strength of movements of the lower limbs and a greater frequency and wider lateral variation of the body center.

Finally, Doi, Furui³⁴ repeated the same method to determine how spontaneous motor patterns observed in neonates (movement magnitude, balance, rhythm, and center of gravity) could predict the autistic risk status based on the M-CHAT score at 18 months. Videos were taken at one time during the maternity stay, between 1 and 4 days postpartum. The authors noted that the performance of logistic regression classifiers was possibly higher in a sleep state, while the difference was not significant. The most critical feature associated with autistic risk status was larger motion frequency in the upper body compared to the lower body and a larger standard deviation in center of gravity movement along the vertical axis (during the awake state).

Aims of our study

This study aims to address the literature gap on the association between abnormal GMs and ASD risk. It is currently unknown whether abnormal GMs observed in neonates only a few days old could inform the risk of developing an ASD. In that view, it is also currently unknown whether recent automated movement analysis based on vision computing captures the same or different motor characteristics than GMs. To explore these two questions, we took advantage of the Chiba Study of Mother and Child Health (C-MACH)³⁷, a birth cohort allowing an observational retrospective study of video analysis of low-risk neonates who also received an assessment of autistic risk status and non-autism-specific general psychopathology at 18 months.

Q1. Are abnormal GMs measured in neonates with a clinician-rated manual instrument associated with a higher likelihood of having autistic risk status at 18 months? If confirmed, this assumption would support the value of assessing GMs in the general procedure for early detection of ASD. In this research, videos of neonates will be retrospectively analyzed using the clinician-rated GMOS-R. The GMOS-R differs from the General Movement Assessment (GMA) used in the previously mentioned studies^{29–31} as it provides a more detailed assessment of motor activities for each body segment. This seems worth considering here, as previous studies have shown that marked differences in the spontaneous motor activities of superior versus inferior limbs, in terms of frequency or amplitude, were consistently associated with a higher autistic risk^{32–34}. We decided to test the relationships for the whole sample and then according to sleep status. Indeed, Doi, Iijima³³ showed that the automated detection of abnormal motion features in sleeping neonates had a higher predictive performance than in awake babies. In addition, several studies have demonstrated in animal models that early motor activity during sleep is crucial for brain development^{38–40}. To indirectly document a specific relation between abnormal GMs in neonates and autistic risk status at 18 months, we also examined the relation of abnormal GMs with a more generic form of non-autism-specific psychopathology assessed with the Strengths and Difficulties Questionnaire (SDQ). Unlike the M-CHAT, the SDQ is not designed to detect autistic risk status; it was therefore used in our analyses to determine the extent to which the association between atypical patterns of general movement is specific to autistic risk or to general psychopathology.

Q2. Does the combination of a GM's manual and automated assessment of motor activities in neonates increase the performance to classify 18-month-old infants as having autistic risk status? As presented above, automated motion extraction analysis is a simple technique based on video with standardized settings, but without the use of external sensors for babies. Manual (i.e., clinician-rated) and automated extraction features

of abnormal motor activities in video may be complementary. For example, some abnormal spontaneous movements, such as microtremors, which occur at very high frequencies and have poor amplitude, can remain invisible to the clinician while being informative. In contrast, other clinically relevant motor “events” can be easily observed by a clinician but remain rare (e.g., synchronized cramps, known to be strongly associated with poor neurological prognosis⁴¹). Combining manual and automated assessments of motor activities enables the generation of new hypotheses using both data-driven and hypothesis-driven approaches.

Materials and methods

Participants

We evaluated 76 babies from the Japanese birth cohort, Chiba Study of Mother and Child Health (C-MACH)³⁷. The dataset included 47 male and 29 female infants. The C-MACH cohort included infants born to mothers recruited before 13 weeks of gestation. Videos were recorded in a hospital located in Chiba Prefecture, when babies were aged 2 ± 0.66 days. This cohort was established as part of a study exploring the effects of genetic and environmental factors on children’s health³⁷. Among the participants, 76 babies had an assessment at 18 months using the M-CHAT. The assessment by SDQ was conducted at five years old. The SDQ scores were available for 65 neonates.

All experiments and analyses were conducted in accordance with relevant guidelines and regulations. The protocol for this study was approved by the Biomedical Research Ethics Committee of the Graduate School of Medicine, Chiba University (ID 451; application date: November 8, 2013). The studies were conducted in accordance with local legislation and institutional requirements (New-Be project, AP-HP number: NIXXXXXHLJ). Informed consent was obtained from all parents or other legal guardians. This study was financed by JSPS KAKENHI Grant Numbers 16H01781 and 15H01584. The first author was funded by a grant from the Mustela Foundation (bourse recherche Action 2022, EF-2022-29883).

Setting

Evaluations of the video of newborns at the maternity ward were blind, meaning that the raters had no clinical information on the babies except for their gender, birth term, birth weight, and height. Each video had a total duration of approximately 20 min. The rater selected a 3-minute extract for a period when the baby displayed a complete sequence of movements. Video of each neonate was assessed either in sleeping or awake state, but not both. When the baby was sleeping, several short segments within the 20-minute video were reviewed to select a final 3-minute sequence. The segment showing the most visible spontaneous motor activity—such as a brief sequence of GMs, an isolated stretch, or a change in body position—without external interference (noise, caregiver handling, or light fluctuation) was selected for scoring. This procedure ensured that the analysis relied on a representative sample of spontaneous movements even during sleep. The infant’s behavioral state was categorized as “awake” or “asleep” based mainly on the presence or absence of eye opening. The infant was considered awake when the eyes were open, with spontaneous limb or trunk movements, and asleep when the eyes were closed, usually with reduced but observable GMs or postural changes. The classification was made visually by the trained rater at the time of segment selection. For the aim of this study, information collected at 18 months in the C-MACH birth cohort was also collected and analyzed (Fig. 1).

Assessments

Each video was scored independently by two raters certified by the GM Trust using the GMOS-R. The GMOS-R was derived from the GMA to provide a valid assessment of spontaneous motor activities in neonates²⁷. The initial GMOS tool was revised to remove items less predictive of neurodevelopmental outcomes. The GMOS-R encompasses 19 items, ranging from 0 (more pathological score) to 2 (more physiological score). The total score represents the sum of the 19 items. A maximum score of 38 indicates the highest quality of movements, which predicts, in theory, positive neurological outcomes²⁸. In line with recommendations, the overall quality of neonates’ motor skills was first rated (i.e., “sequence” item). Then, a detailed assessment by segment (head and trunk, upper limbs, and lower limbs) was rated. In addition to the GMOS-R total score, four subscores are derived: sequence (one item), neck and trunk (two items), upper extremities (eight items), and lower extremities (eight items). In case of discrepancy between the two raters, the videos were reanalyzed. Videos were viewed as often as necessary. In case of persistent disagreement, the most expert rater was followed. The inter-rater reliability depended on the score and ranged between 0.78 (95% CI, 0.68–0.86) and 0.94 (95% CI, 0.90–0.96), indicating good to excellent reliability.

In the automatic analysis, continuous video segments suitable for feature extraction were first extracted from the recordings. Each frame was then binarized to segregate the infant’s body region from the background. Subsequently, a total of 27 features including movement frequency of the whole body characterizing the patterns of the infant’s body movements were quantified according to the algorithm described in^{33,34}, based on the sequence of body-region images across frames. These 27 features were categorized into five categories: movement magnitude, movement balance, movement rhythm, and iCOG (center of gravity) movement (see^{33,34} for details). In the automatic analysis, the data of the infants with small body movements were discarded³⁴. Consequently, automatic features were available only for the remaining 73 neonates.

The M-CHAT was initially developed by Robins, Fein⁴². It was validated for screening toddlers between 16 and 30 months of age to assess risk for ASD, completed by parents of children at 18–24 months of age. The M-CHAT consists of 23 items with binary yes-no responses. The M-CHAT total score represents the number of failed items. This research utilized the validated Japanese M-CHAT version, which has documented good psychometric properties, including internal consistency, inter-rater reliability, test-retest reliability, and concurrent validity with the Childhood Autism Rating Scale- Japanese version score, as well as discriminant validity with later ASD clinical diagnosis⁴³. A positive “at-risk” status was endorsed in children who fail 3 or more

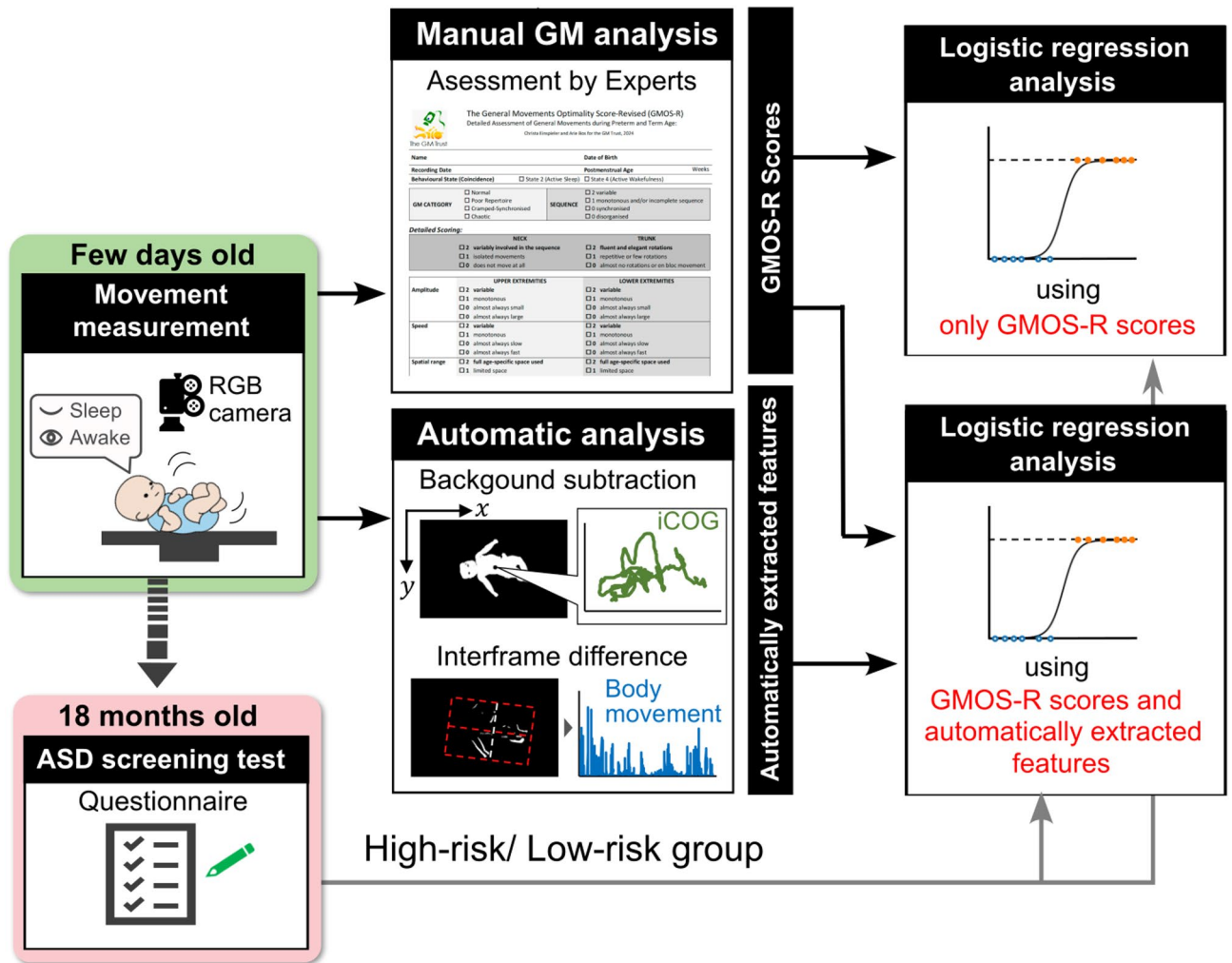


Fig. 1. Study setting.

items total or 1 or more critical items. However, while the M-CHAT is widely used in epidemiological studies as an early screening instrument, especially when a diagnostic assessment is not feasible in large cohorts⁴⁴, it is not a diagnostic tool and has a modest positive predictive value⁴.

The SDQ is a general measure of emotional and behavioral difficulties in youths aged 4–17⁴⁵. It is a 25-item parent-report questionnaire that encompassed five scales of five items each: (i) the emotional problem scale (with score ranging from 0 to 10), (ii) the conduct problem scale (with score ranging from 0 to 10), (iii) the hyperactivity scale (with score ranging from 0 to 10), (iv) the peer problems scale (with score ranging from 0 to 10) and (v) the prosocial scale (with score ranging from 0 to 10). The SDQ total score, also reported as the “Total Difficulties score”, is generated by summing scores from all the scales except the prosocial scale. The resultant score ranges from 0 to 40. While two other amalgamated scales also exist (i.e., externalising score for conduct/hyperactivity scales and internalising score for emotional/peer problems scales), Goodman & Goodman (2009) stipulate that using the four separate scales may add more value in high-risk samples. As no robust evidence supports the predictive power of the SDQ subscales in identifying a clinical diagnosis of ASD⁴⁶, the SDQ was used to examine the extent to which abnormal general movements in newborns were associated with the risk of general psychopathology.

Statistical analysis

We used two-tailed tests and a significance level set at 5%.

The distribution of quantitative variables was summarized using the mean and standard deviation. The distribution of the qualitative variables was described by their levels’ absolute and relative frequencies.

The first main aim was to determine the association between a manual assessment of GMs in neonates and autism risk at 18 months or general psychopathology at 5 years. The associations between the GMOS-R total score and subscores, the M-CHAT total score, and the SDQ total score and subscores were tested using Spearman correlation tests. M-CHAT total score without dichotomization was used in the correlational analysis as a continuous variable. The data of participants with missing values in any M-CHAT items were discarded.

Then, the performance of the GMOS-R score, and in classifying at-risk ASD status based on the dichotomized M-CHAT total score was assessed using the ROC curve and the AUC statistic, along with its confidence intervals. Values greater than 0.5 indicate better performance than random prediction. In line with the method developed by Doi, Furui³⁴, we examined how infants' arousal state during the video influences the classification performance of the GMOS-R.

The second aim was to determine whether combining automated assessment of motor activity with the GMOS-R enhances the classification performance of at-risk status at 18 months. Features extracted by manual and automatic assessment were compressed into PCs after standardization. Only PCs with a proportional explained variance equal to or larger than 5% were retained. PCA of the manual and the automatic assessments were carried out separately, yielding two sets of PCs, i.e., PCs of the manual assessment and PCs of the automatic assessment.

Logistic regression models were estimated using the dichotomous classification of autism risk status based on M-CHAT as the target variable. The first model used only the PCs of the manual assessment as the predictors, whereas the second model used the PCs of both the manual assessment and the automatic assessment as the predictors. Four metrics, i.e., accuracy, F1, recall, and precision, were calculated as the indicators of the classification performance. Comparison was made between the classification model using only the manual assessment PCs and the model using both the manual and the automatic assessment PCs. Then, the AUC was compared with the faster algorithm of the DeLong test proposed by Sun and Xu⁴⁷. The log-likelihood test compared the goodness-of-fit.

Results

Of the 76 babies, 38% were female. Based on the M-CHAT at 18 months, 16 (21%) of them had an autistic risk status and 60 (79%) had not. Table 1 summarizes the main sociodemographic features of the babies.

Manual assessment of GMs in neonates and autism risk at 18 months

As presented in Table 2, the GMOS-R total score and all sub-scores were correlated with the M-CHAT total score. In contrast, no statistically significant associations were found with the SDQ total scores or any of the four SDQ subscores.

Figure 2a (red line) presents the ROC curve for the GMOS-R total score in neonates and the at-risk status at 18 months based on the M-CHAT; the AUC was 0.69 (95% CI, 0.56–0.82). The optimal threshold was 24.5 for a total score out of 38 based on the Youden index, which gives equal weight to sensitivity and specificity, with a sensitivity of 0.88 and a specificity of 0.52.

The GMOS-R total score was associated with the autistic risk status, with an AUC of 0.61 in awake babies (Fig. 2b, red line) and 0.80 in sleeping babies (Fig. 2c, red line).

The logistic regression of three PCs derived from the PCA of the manual assessment showed that only the first PC (i.e., GMA_PC1) remained significantly associated with the ASD status (Table 3). The barplot presented in the Fig. 3 shows the contribution of each GMOS-R items to GMA_PC1. Scores of all the GMOS-R items correlated negatively with the factor score of GMA_PC1. Thus, in other words, the larger factor score of GMA_PC1 indicates generally low scores in the GMOS-R.

Combined manual and automated assessment of GMs in neonates and non-autism-specific psychopathology at 18 months

Figure 2a (green line) presents the ROC AUC score for the combined GM's manual and automated assessment of motor activity in all the neonates, and the at-risk status at 18 months was 0.83. Performance metrics indicate that the addition of the automatic assessment PCs generally improved the classification performance with an accuracy of 0.592, F1 of 0.475, recall of 0.875, and precision of 0.326 for the model without automated features (red line), and accuracy of 0.791, F1 of 0.632, recall of 0.800, and precision of 0.522 for the model with automated features (green line). The log-likelihood test revealed a better fit to the model's data with the automatic assessment PCs than without them, $\chi^2 = 20.03$, $df = 5$, $p = .001$. However, the DeLong test failed to show a significant difference in the AUC between the models ($p = .246$).

As presented in Fig. 2b (green line), the ROC AUC score for the combined manual and automated assessment of GMs in awake neonates and the at-risk status at 18 months was 0.88. Performance metrics indicate that the addition of the automatic assessment PCs markedly improved the classification performance with accuracy of 0.541, F1 of 0.514, recall of 0.900, and precision of 0.360 for the model without automated features (red line),

	All babies (N = 76)	Awaked babies (n = 37)	Sleeping babies (n = 39)
Male	n = 47	n = 22	n = 25
Female	n = 29	n = 15	n = 14
High ASD risk on M-CHAT at 18 months	n = 16	n = 10	n = 6
Low ASD risk on M-CHAT at 18 months	n = 60	n = 27	n = 33
Maternal ages (years), mean (SD)	32.22 (4.58)	32.47 (5.05)	31.94 (3.93)
Gestational Age (Weeks), mean (SD)	39.22 (1.23)	39.39 (1.36)	39.03 (1.03)
Delivery weight (g), mean (SD)	3044.4 (320.6)	3054.6 (364.6)	3032.6 (259.9)

Table 1. Description of the samples.

	M-CHAT at 18 months	SDQ score at 4 years					
		Total score	Emotional Subscore	Hyperactivity Subscore	Conduct problem subscore	Peer problem subscore	Prosocial behavior Subscore
GMOS-R in neonates							
Subscore sequence	T: $rs = -0.45$ $p < .001^{***}$ S: $rs = -0.45$ $p = .005^{**}$ A: $rs = -0.41$ $p = .012^{**}$	T: $rs = -0.06$ $p = .627$ S: $rs = 0.13$ $p = .499$ A: $rs = -0.24$ $p = .173$	T: $rs = 0.03$ $p = .785$ S: $rs = 0.18$ $p = .327$ A: $rs = -0.16$ $p = .380$	T: $rs = -0.01$ $p = .955$ S: $rs = 0.14$ $p = .469$ A: $rs = -0.21$ $p = .234$	T: $rs = -0.07$ $p = .603$ S: $rs = 0.11$ $p = .556$ A: $rs = -0.30$ $p = .086$	T: $rs = -0.12$ $p = .342$ S: $rs = -0.04$ $p = .842$ A: $rs = -0.08$ $p = .665$	T: $rs = 0.19$ $p = .132$ S: $rs = 0.06$ $p = .764$ A: $rs = 0.27$ $p = .120$
Subscore neck and trunk	T: $rs = -0.37$ $p = .001^{**}$ S: $rs = -0.40$ $p = .014^*$ A: $rs = -0.19$ $p = .100$	T: $rs = -0.08$ $p = .545$ S: $rs = 0.03$ $p = .887$ A: $rs = -0.15$ $p = .383$	T: $rs = -0.02$ $p = .902$ S: $rs = 0.11$ $p = .545$ A: $rs = -0.14$ $p = .418$	T: $rs = -0.04$ $p = .741$ S: $rs = 0.12$ $p = .524$ A: $rs = -0.26$ $p = .140$	T: $rs = -0.06$ $p = .644$ S: $rs = -0.10$ $p = .576$ A: $rs = -0.08$ $p = .660$	T: $rs = -0.07$ $p = .605$ S: $rs = 0.04$ $p = .834$ A: $rs = -0.12$ $p = .505$	T: $rs = 0.10$ $p = .438$ S: $rs = 0.08$ $p = .653$ A: $rs = 0.05$ $p = .763$
Subscore upper extremities	T: $rs = -0.34$ $p = .003^{**}$ S: $rs = -0.37$ $p = .022^*$ A: $rs = -0.19$ $p = .248$	T: $rs = 0.02$ $p = .893$ S: $rs = 0.02$ $p = .935$ A: $rs = 0.05$ $p = .783$	T: $rs = 0.02$ $p = .857$ S: $rs = 0.05$ $p = .779$ A: $rs = 0.01$ $p = .938$	T: $rs = 0.07$ $p = .563$ S: $rs = 0.09$ $p = .634$ A: $rs = -0.04$ $p = .804$	T: $rs = -0.01$ $p = .943$ S: $rs = -0.05$ $p = .805$ A: $rs = -0.05$ $p = .762$	T: $rs = -0.03$ $p = .806$ S: $rs = -0.02$ $p = .903$ A: $rs = 0.09$ $p = .623$	T: $rs = 0.15$ $p = .217$ S: $rs = 0.14$ $p = .444$ A: $rs = 0.07$ $p = .695$
Subscore lower extremities	T: $rs = -0.39$ $p = .001^{**}$ S: $rs = -0.46$ $p = .004^{**}$ A: $rs = -0.22$ $p = .188$	T: $rs = -0.03$ $p = .828$ S: $rs = 0.06$ $p = .751$ A: $rs = -0.13$ $p = .469$	T: $rs = 0.05$ $p = .691$ S: $rs = 0.05$ $p = .786$ A: $rs = 0.03$ $p = .877$	T: $rs = -0.03$ $p = .820$ S: $rs = 0.11$ $p = .553$ A: $rs = -0.24$ $p = .174$	T: $rs = -0.05$ $p = .677$ S: $rs = 0.08$ $p = .673$ A: $rs = -0.22$ $p = .204$	T: $rs = -0.03$ $p = .943$ S: $rs = 0.01$ $p = .941$ A: $rs = 0.03$ $p = .845$	T: $rs = -0.20$ $p = .108$ S: $rs = 0.09$ $p = .627$ A: $rs = 0.22$ $p = .204$
Total GMOS-R	T: $rs = -0.40$ $p < .001^{***}$ S: $rs = -0.44$ $p = .007^*$ A: $rs = -0.25$ $p = .133$	T: $rs = -0.01$ $p = .941$ S: $rs = 0.01$ $p = .950$ A: $rs = -0.07$ $p = .713$	T: $rs = 0.03$ $p = .803$ S: $rs = 0.04$ $p = .841$ A: $rs = 0.00$ $p = .971$	T: $rs = 0.01$ $p = .916$ S: $rs = 0.08$ $p = .654$ A: $rs = -0.20$ $p = .268$	T: $rs = -0.04$ $p = .780$ S: $rs = -0.01$ $p = .971$ A: $rs = -0.15$ $p = .385$	T: $rs = -0.03$ $p = .839$ S: $rs = -0.02$ $p = .929$ A: $rs = 0.05$ $p = .772$	T: $rs = 0.18$ $p = .153$ S: $rs = 0.09$ $p = .629$ A: $rs = 0.16$ $p = .375$

Table 2. Correlations between GMOS-R in neonates and MCHAT at 18 months and SDQ at 4 years. T: total sample, S: sleeping babies only, A: awake babies only *** $p < .001$, ** $p < .005$, * $p < .05$

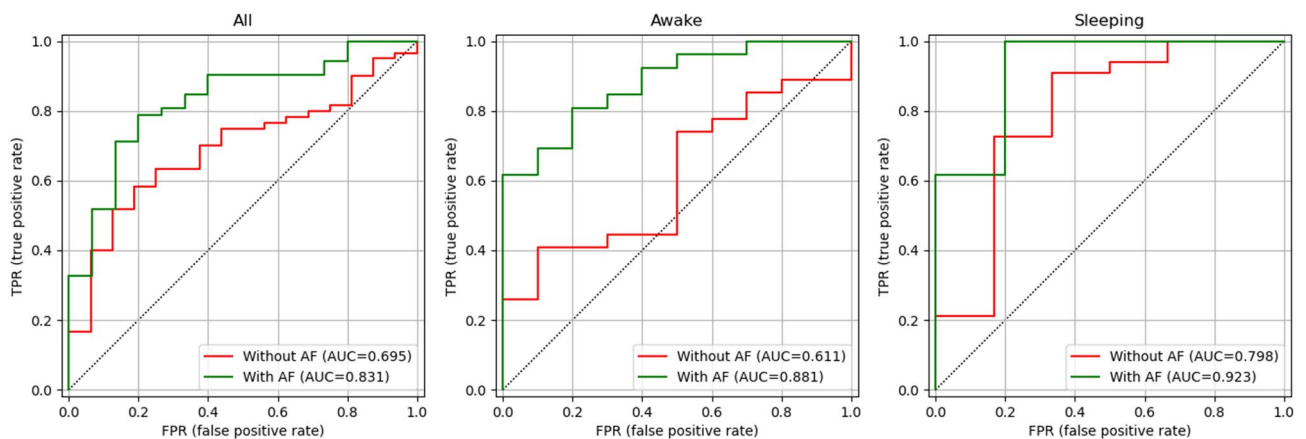


Fig. 2. a, b, c. ROC curves for the association between the GMOS-R total score in neonates and at-risk status at 18 months (a) whole sample, (b) awake babies, (c) asleep babies. AF = Automatic features.

Predictor variable	β	SE	Z	p
Intercept	-1.44	0.31	-4.642	
GMA_PC1	0.583	0.283	2.063	0.039*
GMA_PC2	-0.217	0.660	-0.329	0.742
GMA_PC3	-0.366	0.864	-0.424	0.672

Table 3. Logistic regression of autistic risk status based on extracted PCs with only manual assessment. GMA = General Movement Assessment, LL = Lower Limb, UL = Upper Limb.

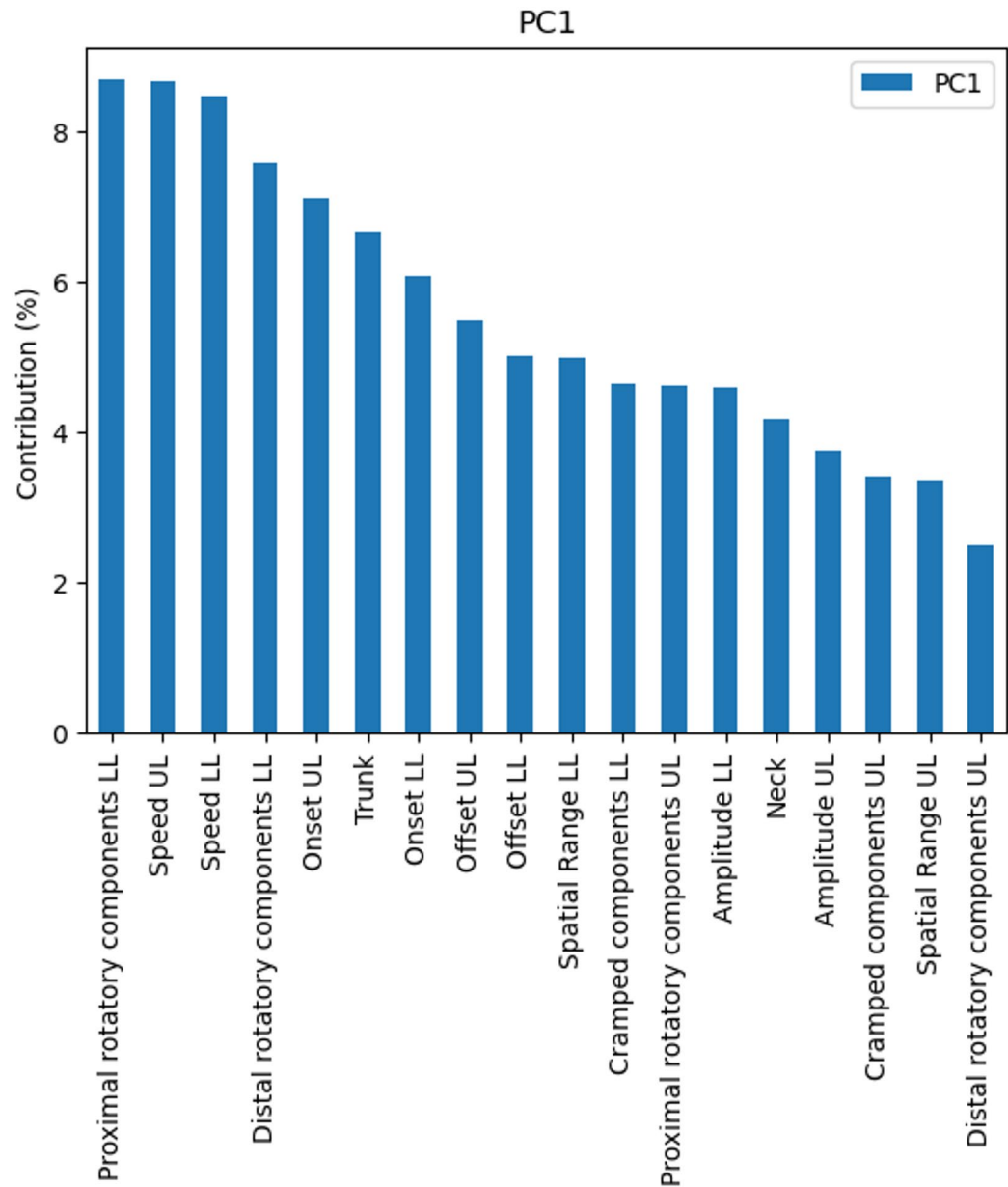


Fig. 3. Contribution of the items associated with the principal component GMA_PC1.

and accuracy of 0.722, F1 of 0.667, recall of 1.000, and precision of 0.500 for the model with automated features (green line). The log-likelihood test revealed a better fit to the model's data with the automatic assessment PCs than without them, $\chi^2 = 15.06$, $df = 5$, $p = .010$. The difference in the AUCs approached but failed to reach significance, $p = .070$.

As presented in Fig. 2c (green line), the ROC AUC score for the combined manual and automated assessment of GMs in asleep neonates and the at-risk status at 18 months was 0.92. Performance metrics indicate that the addition of the automatic assessment PCs slightly improved the classification performance with accuracy of 0.872, F1 of 0.615, recall of 0.667, and precision of 0.571 without automated features (red line), and accuracy of 0.968, F1 of 0.889, recall of 0.800, and precision of 1.000 with automated features (green line). The log-likelihood test revealed a better fit to the model's data with the automatic assessment PCs than without them, $\chi^2 = 14.89$, $df = 4$, $p = .005$. There was no difference in AUC between the models, $p = .340$.

As presented in Table 4, for combined analyses, only two PCs of the automatic features (i.e., AF_PC3 and AF_PC5) were associated with ASD risk. Contribution of items for each PC is detailed in Fig. 4.

Discussion

Summary of main results

Although exploratory, given the sample size and the number of infants at autistic risk, our finding supports the relevance of considering abnormal motor patterns in neonates as an early marker of autistic risk. Regarding our

first research question, we found that the GMOS-R total score and subscores significantly predicted the autistic risk status according to the M-CHAT, but not the general psychopathological status according to the SDQ.

In the manual assessment of GM, the factor score of GMA_PC1 was the most informative feature in predicting ASD risk. The contribution to GMA_PC1 was numerically larger for limb movement speed and rotatory components than for the other GMOS-R items. However, this tendency was not particularly prominent. Additionally, auxiliary analyses revealed that all GMOS-R items were negatively correlated with the factor score of GMA_PC1. These results suggest that the factor score of GMA_PC1 can be interpreted as representing “the global poorness of general movement”. Taken together, the association between autistic risk status and GMA_PC1 indicates the usefulness of assessing global motion patterns in neonates for the early screening of ASD risk. All GMOS-R subscales, as well as the total score, showed significant correlations with the M-CHAT score. This observation is consistent with the significant association between GMA_PC1 and the autistic risk status assessed by MCHAT, in the sense that the status of all aspects of infant body motion may contribute to the assessment of ASD risk.

Regarding our second research question, we found an improvement in the classification performance with the addition of the automatically extracted features for both awake and asleep babies. This improvement came mainly from incorporating information about the imbalance in motion strength between the upper and lower limbs (AF_PC3). These findings extend to neonates the results from previous studies, where atypical movement patterns were observed by trained professionals in older samples or with a broader age range (mostly 0–5 months)^{29–31}.

The sensitivity at our threshold chosen for the GMOS-R in predicting autistic risk based on M-CHAT at 18 months was 88%, which was slightly higher than the sensitivity of GMA at 70% reported by Phagava, Muratori³⁰ in older infants during the period of writhing movements, and the sensitivity at 68% reported in the review of Einspieler, Sigafos²⁹ who included the cases published by Phagava.

In our study, the specificity of the GMOS-R in predicting autistic risk status based on M-CHAT at 18 months was 50%. Zapella et al. reported a higher specificity at 88% for the GMA in only 18 babies between 1 and 6 months. One can easily imagine that the level of specificity of GMs increases when the baby grows up, considering the progressive brain maturation and the disappearance of transient cerebral structures involved in early sensory-motor activity⁴⁸. This assumption is consistent with the literature on GMs that stipulates that the writhing period has good sensitivity, and the fidgety period has a better specificity for neurological outcomes^{20,22,25}.

As presented in Table 2, the four GMOS-R subscores were significantly correlated with the M-CHAT at 18 months, in a comparable range. Compared to the original GMA instrument, the additional features of the body segments assessed by the GMOS-R provide a more complete picture of abnormal motor patterns. Another line of evidence for the one-dimensionality of GMs is provided by principal component analysis. As presented in Table 3, ASD risk was associated with GMA_PC1, which accounts for a substantial contribution from nearly all GMOS-R items. This GMA_PC1 could then be interpreted as a reflection of an “overall quality of body movement”.

How could we explain the association between the “*Neck and Trunk*” subscore of the GMOS-R and the M-CHAT score at 18 months suggested by our sample? It is worth noting that the progressive emergence of a stable body axis in infants with typical development underpins subsequent psychomotor development^{49,50}. For example, it is essential to stabilize the head and then the shoulders to acquire an optimal function of the upper limbs^{51,52}. A comparable phenomenon is observed in the stability of the pelvis, which enables proper use of the lower limbs. The lower frequency of rotations and the less fluent and elegant features of these movements in neonates later regarded as having an autistic risk risk in our study are consistent with Doi, Furui³⁴. These authors found more variations in babies’ body axes and the center of gravity. The rotational movements of the babies in the head-trunk axis are a key element during typical development, providing dynamic stability of the body axis. Caruso, Gila³² also found that babies at high risk for ASD had greater velocity and acceleration of the “centroid of motion,” which is consistent with jerky movements and lower stability of the body axis.

The association between the “*Upper extremities*” subscore of the GMOS-R and autistic risk status, as suggested by our sample, is consistent with previous observations of atypical hand and arm movement patterns in babies at risk of NDDs^{53,54}. Babies with autistic risk status in our study had more frequent jerky movements and a lack of rotational components. These atypical upper-limb movement patterns could impair the ability to

Predictor variable	β	SE	Z	p-value
Intercept	-1.756	0.44	-3.992	
GMA_PC1	-0.193	0.44	-0.441	0.659
GMA_PC2	0.924	1.15	0.802	0.422
GMA_PC3	-2.658	1.49	-1.788	0.074
AF_PC1	0.180	0.13	1.415	0.157
AF_PC2	-0.215	0.18	-1.227	0.220
AF_PC3	0.660	0.27	2.476	0.013*
AF_PC4	0.445	0.29	1.536	0.125
AF_PC5	0.729	0.34	2.142	0.032*

Table 4. Logistic regression of autistic risk status based on extracted PCs with both manual and automated assessment. AF = automatic features.

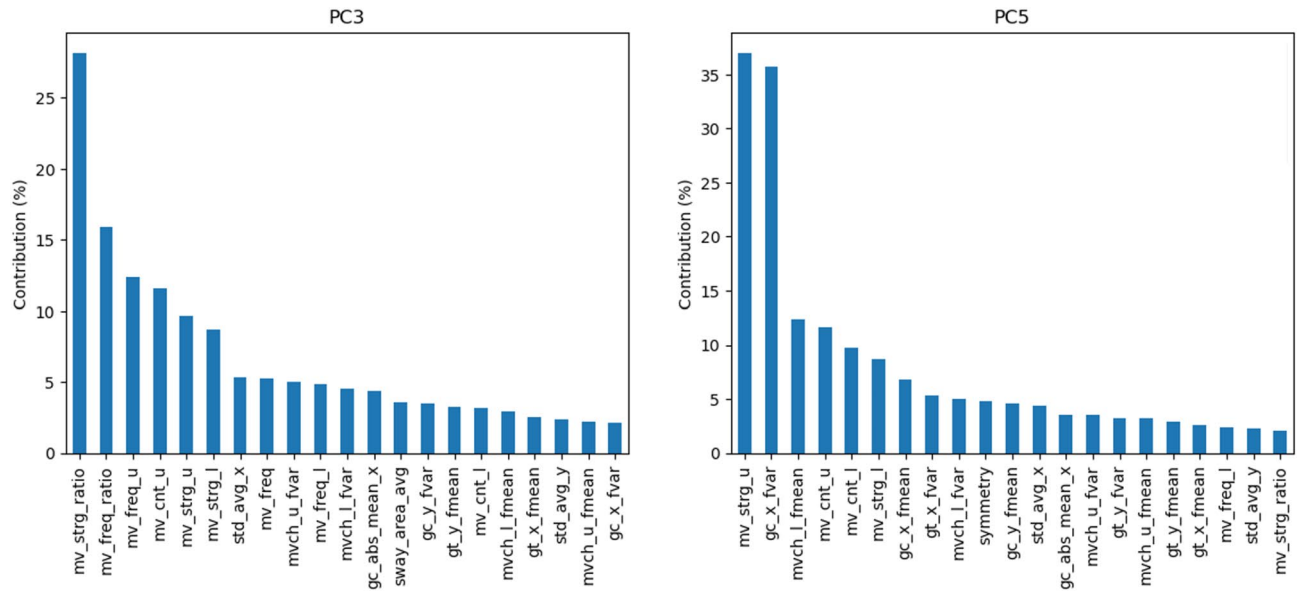


Fig. 4. Contribution of the items associated with PC3 and PC5. *Note.* mv_freq: Movement frequency mv_freq_u: Movement frequency in upper body mv_freq_l: Movement frequency in lower body mv_strg_u: Movement strength in upper body mv_strg_l: Movement strength in lower body mv_cnt_u: Movement count in upper body mv_cnt_l: Movement count in lower body mv_freq_ratio: Ratio of movement frequency between upper and lower body mv_strg_ratio: Ratio of movement strength between upper and lower body symmetry: Symmetry/coordination between upper and lower body mvch_u_fmean: Mean power frequency in upper body mvch_u_fvar: Standard deviation around mean power frequency in upper body mvch_l_fmean: Mean power frequency in lower body mvch_l_fvar: Standard deviation around mean power frequency in lower body gc_x_fmean: Mean power frequency of iCOG velocity along x axis gc_x_fvar: Standard deviation of iCOG velocity along x axis gc_y_fmean: Mean power frequency of iCOG velocity along y axis gc_y_fvar: Standard deviations of iCOG velocity along y axis gt_x_fmean: Mean power frequency of iCOG fluctuation along x axis gt_x_fvar: Standard deviations of iCOG fluctuation along x axis gt_y_fmean: Mean power frequency of iCOG fluctuation along y axis gt_y_fvar: Standard deviations of iCOG fluctuation along y axis gc_abs_mean_x: Mean absolute value of iCOG velocity along x axis gc_abs_mean_y: Mean absolute value of iCOG velocity along y axis std_avg_x: Standard deviation of iCOG fluctuation along x axis std_avg_y: Standard deviation of iCOG fluctuation along y axis sway_area_avg: Area covered by the outermost circumference of iCOG trajectory.

bring the hand toward the midline, a milestone in typical development. For example, the Standardized Infant Neurodevelopmental Assessment included distinct items to rate the infant's ability to look at their hands and bring them to their mouth². We also report exaggerated fidgety movements in the upper limbs (referred to as abnormal fidgety) among infants at risk of ASD, consistent with other authors^{31,32}. For some authors, the persistence of these atypical movement patterns after five months could disturb the appearance of goal-directed movements and predict stereotypical movements, which are so common in ASD children⁵⁴.

In our study, the sleeping status was associated with better predictive performance of the GMOS-R, in line with Doi, Furui³⁴, who showed better predictive performance of their models in sleeping versus. non-sleeping babies. One can hypothesize that spontaneous movements are closer to sleep in their involuntary nature². Perhaps the baby's state of alertness can influence the quality of his movements by moving them away from their spontaneous character (spontaneous meaning not being influenced by the environment). Another hypothesis is related to the very level of the noisy environment in the maternity ward that may influence, to a lesser degree, the GMs if the baby was sleeping. However, studies in animal models have repeatedly shown the importance of motor activities during sleep in early brain development^{38,40}. Therefore, it is likely that differences found between motor activities in awake and asleep babies are also significant in humans.

The combination of automatic features with the GMOS-R significantly improved the goodness of fit of the classification models. The benefit of combining manual and automated assessment of spontaneous movements was more marked for asleep babies. Interestingly, for combined analyses, only PCs of the automatic features (AF_PC3 and AF_PC5) were associated with autistic risk status. Analysis item-by-item showed that the movement strength ratio (relative strength of the upper limb movement compared to the lower limb movement) significantly contributed to AF_PC3. AF_PC3 should be interpreted as an "Imbalance in Movement Strength along the vertical axis." For AF_PC5, the largest contribution was from the movement strength in the upper limb ("mv_strg_u") and the standard deviation of the spectral power in the time-series of the center of gravity along the x-axis ("gc_x_fvar"). In particular, "gc_x_fvar" can be interpreted as an indicator of rhythmicity. The larger this index, the less rhythmic the movement is.

Strengths and limitations

The strengths of this study lie in its investigation of whether ASD risk is associated with an expert's assessment of GMs using a simple method in neonates with an 18-month follow-up period. Several limitations need to be considered when interpreting these findings.

Firstly, the sample size was limited because of the inherent difficulty in recruiting neonates. The 76 individuals included only 16 infants with a positive autistic risk status. Secondly, the measuring instrument for the primary outcome (i.e., the « ASD risk » status) was the M-CHAT questionnaire completed by parents. While largely consensual among clinical researchers⁴⁴, its predictive performance remains limited, with a positive predictive value estimated at 58%⁴. As the primary goal of the M-CHAT was to maximize sensitivity, a high false positive rate exists. One may also regret that the follow-up period was limited to 18 months, and the structured M-CHAT Follow-up Interview, created to increase predictive validity, was not used here. While a significant number of children who fail the M-CHAT will not be diagnosed with an ASD, they are at risk of other NDDs. For this, it would have been interesting to have more information on these babies' evolution in terms of clinical, cognitive, and developmental profiles with a comprehensive assessment of ASD/other NDD at 3 years old. A substantial attrition rate can explain why only a subgroup of the neonates completed the SDQ at five years.

Thirdly, the study design (retrospective video analysis) could only provide one assessment point for GMs. The evolution in the predictive performance of the GMOS-R with time cannot be determined. GMs' very nature changes during infants' typical development^{20,21}, so the predictive performance of GMOS-R items could.

Fourthly, selection bias cannot be excluded, given the specific characteristics of the Chiba cohort participants. Replication of these findings is therefore needed in distinct contexts, including samples enriched in neonates at high ASD risk due to genetic factors (e.g., siblings) and/or environmental factors (e.g., severe obstetrical or neonatal complications).

Finally, given the lack of cross-validation or validation on a separate dataset, the observed statistically significant relationships may be overestimated due to overfitting in the data used for machine learning. The current analysis should be regarded as inferential rather than predictive, and replication is necessary before any generalization can be made.

Clinical and research implications

These findings stress the interest in considering atypical movement patterns, specifically GMs, to detect infants at autistic risk status. The main contribution of this research is the replication in babies only a few days old of previous works on the association between GMs and ASD risk²⁹⁻³¹. The GMOS-R questionnaire offers an operational instrument to assess subtle signs of atypical motor development in babies, reported for decades in the literature^{13,51,55}. If these results were confirmed in other cohorts, using a prospective method, the assessment of GMs could be included in the clinical strategy of very early detection of ASD risk alongside other recommended methods⁵⁶. The GMOS-R can be viewed as complementary to other methods, as the latter mainly focuses on the infant's abnormal communication or social interactions observed later in development, but not on abnormal motor patterns per se. Neonates with abnormal GMs could receive specific support to prevent the risk of poor neurodevelopmental outcomes, including referral to the local structures for early detection, diagnosis, and intervention for NDDs, where close monitoring of the infant's developmental acquisitions is provided.

Future research could investigate the impact of motor-based interventions on the progression of such atypical motor patterns and, ultimately, on ASD risk. For instance, some protocols suggest that parental involvement in daily sessions of playful motor activities with their 0- to 2-month-old infants, accompanied by songs, could influence the development of general movements^{57,58}. Another research question could investigate whether the motor impairments observed in autism are linked to upstream disturbances that also impact other areas of the central nervous system, such as the sensory system (e.g., hypersensitivities) and the autonomic nervous system (e.g., digestive and sleep troubles).

Conclusion

The patterns of atypical spontaneous motor activity, measured with the GMOS-R in video-recorded neonates, significantly predicted autistic risk status, as assessed by the M-CHAT score at 18 months, but did not predict other forms of general psychopathology assessed by the SDQ. Combining automated measures of neonates' motor activities with the GMOS-R manual assessment improves the classification of ASD risk, supporting the importance of motor activity dimensions that may not be readily observable to clinicians. This finding serves as proof of concept, demonstrating that general movement measurement has the potential to enhance early detection of ASD risk in neonates.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Study concept and design: AB, CSG, DC, MY, KSh, KSa, CM, AF, TT, HD Acquisition of data: AB, CSG, IH, MDC, PG, MC, MCL, OLE, MY, KSh, KSa, CM, AF, TT Interpretation of data: AB, CSG, IH, MDC, PG, MC, MCL, OLE, HP, GB, DC, SA, MY, KSh, KSa, CM, AF, TT, XB, HDDrafting the manuscript: AB, CSG, HP, GB, DC, XB, HDCritical revision of the manuscript for important intellectual content: CSG, HP, GB, SA, DC, XB, HDFinal draft: All authors.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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