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3 Title

- 4 From brain to education through machine learning: Predicting literacy and
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19 From brain to education through machine learning: 20 Predicting literacy and numeracy skills from neuroimaging data 21 22 Tomoya Nakai^{1,2*}, Coumarane Tirou¹, Jérôme Prado^{1*} 23 24 ¹Lyon Neuroscience Research Center (CRNL), INSERM U1028 - CNRS 25 UMR5292, University of Lyon, 69500 Bron, France. 26 ²Araya Inc., Tokyo, Japan 27 *To whom correspondence may be addressed. 28 Email: nakai.tomoya@neuro.mimoza.jp, jerome.prado@univ-lyon1.fr 29 Keywords: education, development, neuroscience, machine learning, learning 30 disability 31 32 Abstract 33 The potential of using neural data to predict academic outcomes has always 34 been at the heart of educational neuroscience, an emerging field at the crossroad of psychology, neuroscience and education sciences. Although this 35 36 prospect has long been elusive, the exponential use of advanced techniques in 37 machine learning in neuroimaging may change this state of affairs. Here we 38 provide a review of neuroimaging studies that have used machine learning to 39 predict literacy and numeracy outcomes in adults and children, both in the context of learning disability and typical performance. We notably review the 40 41 cross-sectional and longitudinal designs used in such studies, and describe how 42 they can be coupled with regression and classification approaches. Our review highlights the promise of these methods for predicting literacy and numeracy 43 44 outcomes, as well as their difficulties. However, we also found a large variability 45 in terms of algorithms and underlying brain circuits across studies, and a 46 relative lack of studies investigating longitudinal prediction of outcomes in young children before the onset of formal education. We argue that the field needs a 47 48 standardization of methods, as well as a greater use of accessible and portable 49 neuroimaging methods that have more applicability potential than lab-based 50 neuroimaging techniques.

51 Introduction

52 The past few decades have seen a rapid increase in our understanding of how the brain changes over development and learning, leading a number of 53 54 neuroscientists to consider implications of these findings for education. This has 55 led to the emergence of the field of educational neuroscience (Ansari & Coch. 56 2006; Goswami, 2004, 2006), defined in a recent review (Thomas et al., 2019) 57 as "an interdisciplinary research field that seeks to translate research findings 58 on neural mechanisms of learning to educational practice and policy". However, 59 this general endeavor has not been unchallenged. Critics have notably claimed 60 that neuroscience findings are too remote from the classroom to be informative 61 and to have practical implications for children or educational systems (Bruer, 62 1997). Others have argued that behavioral measures are more practical to 63 characterize children's cognitive capacities than neuroimaging measures 64 (Bowers, 2016).

In an early review, Gabrieli et al. (2015) argued otherwise and 65 66 suggested that brain measures obtained through neuroimaging techniques may be useful for predicting future academic outcomes and therefore help design 67 interventions, as well as for evaluating the success of interventions. A relatively 68 69 limited number of studies were available at the time of Gabrieli et al.'s review. 70 However, significant progress has since been made in both neuroimaging and 71 machine learning techniques. The term "machine learning" refers here to a set 72 of computational methods that involve the development of algorithms and 73 statistical models relying on patterns and inference derived from data. These 74 computational methods typically use past information to improve their 75 performance or to make accurate predictions over time (Mohri et al., 2012). 76 Because these technological advances are changing the landscape of what 77 may be possible in terms of the prediction of outcomes from neural signals, we 78 aimed here to provide an updated review of recent advances in neuroscience and machine learning that may have application to both education and the 79 80 treatment of neurodevelopmental disorders. Though the present review 81 primarily focuses on the methodological framework, challenges, and main 82 findings from these studies, we will also end by discussing the potential practical applications of this line of research. 83 84 The present review largely focuses on findings in the domains of literacy 85 and numeracy skills (and associated disorders) for two reasons. First, literacy

86 and numeracy skills are considered fundamental to modern science and

87 technologies, and difficulties in acquiring these abilities may negatively impact 88 academic attainment and financial well-being (Estrada-Mejia et al., 2016). 89 Predicting reading and mathematical difficulties in children has therefore critical 90 societal relevance. Second, literacy and numeracy are probably the academic 91 domains for which the most progress has been made in developmental 92 cognitive neuroscience over the past decades. We will, however, also include in 93 our review several studies that have focused on other cognitive factors relevant 94 to education. Finally, we will highlight future directions for studies aiming to 95 apply machine learning to neural data in order to predict and improve 96 educational outcomes.

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Predicting educational outcomes from brain activity: methodological considerations

100 Gabrieli et al. (2015) pointed out that the term "prediction" can have at least 101 three different meanings in studies. In its weakest form, the term might be used 102 to describe a correlation between two sets of variables obtained at the same 103 time point. In a slightly stronger form, it can also be used to describe a 104 correlation between two sets of variables obtained at different time points. In its 105 strongest form, "prediction" may describe a model generalization to out-of-106 sample individuals, which typically relies on machine learning. This third 107 meaning is arguably the closest to the definition of a "prediction" in common 108 language. Studies demonstrating an out-of-sample generalization have also the 109 most practical relevance because they suggest that a model would be 110 applicable to novel data that are not specific to a given sample.

111 The present review exclusively focuses on the term "prediction" as 112 describing generalization to out-of-sample individuals, and therefore only 113 includes studies demonstrating such generalization. As a side note, not all 114 neuroimaging studies using machine learning techniques are relevant to the 115 question of individual differences in academic performance, learning, or 116 development. For instance, studies may use machine learning to test 117 differences in spatial distributions of neural activity across tasks (Nakai et al., 118 2023). These studies are not included in the present review either. 119 Broadly speaking, previous neuroimaging studies using machine learning 120 to predict educational outcomes can be divided into two categories. The first 121 category (Figure 1, top row) encompasses studies using a cross-sectional

122 design, such that different participants are evaluated at one (T1) or several time

123 points (T1 and T2). The second category (Figure 1, bottom row) includes 124 studies using a longitudinal design, such that the same participants are 125 evaluated at different time points (T1 and T2). These time points can be 126 separated by days, weeks or even years. Note that cross-sectional and 127 longitudinal studies may use supervised learning to either predict a continuous 128 distribution of achievement (e.g., reading, math) scores from brain activity or 129 discrete categorical labels such as presence or absence of learning disability. 130 While the former relies on regression analyses (Figure 1, left column), the latter 131 involves classification analyses (Figure 1, right column) (Bishop, 2006).

132 Note that the three typical meanings of "prediction" in Gabrieli et al. 133 (2015) can be categorized along the dimensions of "in-sample correlation vs. 134 out-of-sample prediction" and "cross-sectional vs. longitudinal". That is, the first 135 two meanings are similar in that they both focus on in-sample correlation but 136 are different because one uses a cross-sectional design and the other a 137 longitudinal design. The third meaning (out-of-sample prediction) can also be 138 applied to both cross-sectional and longitudinal data (Figure 1). In both cases, machine learning models are trained with a subset of samples, and their 139 140 generalizability is tested with left-out samples.

141 Regression and classification analyses use different analytic strategies. 142 For instance, regression analysis as it is applied to a cross-sectional design 143 (Figure 1, upper left cell) relies on the generation of a predictive model based 144 on the relation between brain and behavioral data across participants from the 145 training set at T1. The trained model is then used to predict behavior from brain 146 data in left-out participants, also at T1. Regression analysis as it is applied to a 147 longitudinal design (Figure 1, bottom left cell) relies on the generation of a 148 predictive model based on the relation between brain data at T1 and behavioral 149 data at T2 across participants from the training set. The trained model is then 150 used to predict behavior at T2 from brain data at T1 in left-out participants. 151 Classification analysis as it is applied to a cross-sectional design (Figure 1, 152 upper right cell) relies on an association between a discrete categorization of 153 participants from the training set according to behavioral labels defined at T1 154 and their brain data at T1. This trained model is then used to assign labels to 155 left-out participants based on their specific brain data, also at T1. Classification 156 analysis as it is applied to a longitudinal design (**Figure 1**, bottom right cell) 157 relies on an association between a discrete categorization of participants from 158 the training set according to behavioral labels defined at T2 (e.g., typically

developing or learning disabled) and their brain data at T1. This trained model is
then used to assign labels to left-out participants based on their specific brain
data at T1. The specific methodologies underlying these analyses are
discussed in a later section (see **Studies use a range of machine learning methods**). The present study does not include data from human or animal
subjects and does not require approval from the ethics committee or informed
consent.





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- 168 Figure 1. Schematic chart outlining the methodology used in
- 169 neuroimaging studies reviewed here. Studies can be categorized into
- 170 following a cross-sectional or a longitudinal design (rows), as well as a
- 171 regression or a classification approach (columns). T1, time point 1; T2, time
- point 2. Note that, although cross-sectional design can be applied to multiple
- 173 time points, we only describe the case of T1 to avoid confusion with the
- 174 longitudinal design. Furthermore, we also simplified the description of the

- 175 longitudinal design by excluding cases of using differences of behavioral data
- 176 (T2 T1) as explained variables. Labels #1 and #2 indicate discrete
- 177 categorization of individuals (e.g., typically developing or learning disabled).
- ANN, artificial neural network; DA, discriminant analysis; kNN, k-nearest
- 179 neighbors; NBC, naïve Bayes classifiers; RF, random forest; SVM, support
- 180 vector machine; SVR, support vector regression.
- 181

182 Can neuroimaging studies predict literacy skills?

183 A number of cross-sectional (Table 1) and longitudinal (Table 2) neuroimaging 184 studies have attempted to use brain data to predict literacy skills (see 185 Supplementary Information for the selection criteria of articles and the 186 methodology used to generate the tables). For example, using regression in a 187 cross-sectional design, He et al. (2013) showed that gray matter (GM) structural 188 MRI (sMRI) data from adult participants could predict various language abilities 189 (phonological decoding, form-sound association, and naming speed) 190 decomposed from a set of behavioral measures. Xu et al. (2015) further used 191 fractional amplitude of low-frequency fluctuations (ALFF) in resting fMRI (rest-192 fMRI) data to predict reading test scores (efficiency of mapping orthography to 193 semantic) of adult participants. Subsequent studies have focused on large 194 datasets of adult participants provided by the Human-Connectome Project 195 (HCP) (Van Essen et al., 2013). These studies used either the Oral Reading Recognition Test and/or Picture Vocabulary Test combined with different types 196 197 of brain data: sMRI (Cui et al., 2018; Kristanto et al., 2020), functional 198 connectivity (FC) of rest-fMRI (Kristanto et al., 2020; Yuan et al., 2023), 199 diffusion MRI (dMRI) (Kristanto et al., 2020), and task-fMRI (language, working 200 memory, and motor tasks) (Tomasi & Volkow, 2020). Together, these studies 201 show that it is possible to predict individual differences in literacy skills with 202 different sources of neuroimaging data, indicating that such skills are related to 203 brain data over multiple dimensions.

Other studies have attempted to use neuroimaging data to classify between participants with and without dyslexia, a specific learning difficulty in word recognition, word decoding, and spelling abilities, with otherwise normal intelligence (American Psychiatric Association et al., 2013). For example, Tamboer et al. (2016) classified adults with and without dyslexia using sMRI (GM) data. Cui et al. (2016) and Joshi et al. (2023) further showed that such 210 classification was not limited to adults based on dMRI and sMRI data. respectively. Using sMRI (GM) data, but with a larger sample size including 211 212 children from three different countries (130 children with dyslexia and 106 213 typically-developing children), Płoński et al. (2017) replicated successful 214 dvslexia classification. Finally, some studies have reported successful 215 classification between children with and without dyslexia based on task-216 electroencephalography (EEG) with word comprehension (Zainuddin et al., 217 2018) and auditory stimuli listening (Formoso et al., 2021), and resting 218 magnetoencephalography (MEG) signals (Dimitriadis et al., 2018). Although 219 many of the studies above rely on rest-fMRI or sMRI data, more recent studies 220 have also used task-fMRI data. For example, Mascheretti et al. (2021) classified 221 dyslexic from non-dyslexic children using a visual detection task, whereas 222 Tomaz Da Silva et al. (2021) used a word-reading task. Finally, Zahia et al. 223 (2020) used three different reading tasks to classify children with dyslexia, 224 monocular vision (due to ocular motility disorders), and control groups.

225 Studies have also attempted to distinguish between different subtypes 226 of language-related disorders and language proficiency levels. Bailey et al. 227 (2016) were able to distinguish children with dyslexia from those with specific 228 reading comprehension deficits (SRCD) based on their sMRI (GM) data. SRCD 229 differs from dyslexia in that affected children have difficulty in reading 230 comprehension despite adequate phonemic decoding (Landi & Ryherd, 2017). Cignetti et al. (2020) and Nemmi et al. (2023) classified between children with 231 232 dyslexia and with developmental coordination disorder (DCD) using rest-fMRI and sMRI (GM and white matter [WM]) data. Zare et al. (2016) and Yu et al. 233 234 (2022) classified whether children's families had a history of dyslexia using rest-235 EEG and rest-fMRI data, respectively. One study has also used functional near-236 infrared spectroscopy (fNIRS) study to classify between higher and lower second language proficiency groups (Lei et al., 2020). Barranco-Gutiérrez 237 238 (2020) classified between adults who are native English speakers and those 239 who learned English as a second language. Zhang et al. (2023) classified 240 second language (English) proficiency levels (high, moderate, low) of Chinese 241 speakers and further predicted listening comprehension scores using fMRI with 242 a story listening task. Mossbridge et al. (2013) found that good and poor 243 readers were separable using EEG data during a sentence comprehension 244task.

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Study	Target ability/groups	Sample size	Mean age/age	Data type	Technique	Cross- validation	Max prediction accuracy	Brain areas	Selection method of brain areas
He et al. (2013)	Phonological decoding, form-sound association, naming speed	253	21.5	sMRI (GM)	Linear SVR	10-fold CV	Phonological decoding, <i>r</i> = 0.26; form-sound association, <i>r</i> = 0.23; naming speed, <i>r</i> = 0.24	Phonological decoding, 4 regions including L. SPL and precuneus; form- sound association, 9 regions in the temporal cortex and hippocampus; naming speed, 11 regions in the frontal, temporal, and parietal cortices	Searchlight
Mossbrid ge et al. (2013)	Subjects with good or poor reading scores	28	18-29	Task-EEG (sentence comprehensi on)	RF	Repeated selection of 35% of subjects (1000 times)	88.3%	Medial frontal channel	Weight values
Xu et al. (2015)	Reading scores	263	22.1	rest-fMRI (ALFF)	Linear regression	4-fold CV	r = 0.24	Bilateral PreCG, STG	Predetermined ROIs. Non-independent
Bailey et al. (2016)	Dyslexia, SRCD	41 (14 dyslexia, 11 SRCD, 16 TD)	Dyslexia, 12.5; SRCD, 11.5; TD, 11.9	sMRI (GM)	Linear SVM	LOOCV	92.5% (SRCD vs. TD)	Large portions of the frontal, temporal, parietal, occipital cortices, subcortex and cerebellum	Weight values
Cui et al. (2016)	Dyslexia	61 (28 dyslexia, 33 TD)	Dyslexia, 11.6; TD, 11.8	sMRI (WM), dMRI (FA, mean, axial, radial diffusivity)	Linear SVM, Logistic regression	LOOCV	83.6% (SVM)	43 (SVM) and 40 (Logistic regression) connections across the brain	CV within training data
Tamboer et al. (2016)	Dyslexia	First sample: 49 (22 dyslexia, 27 TD); second sample: 876 (60 dyslexia, 816 TD)	First sample, dyslexia, 20.7; TD, 20.3; second sample, dyslexia, 22.5; TD, 22.9	sMRI (GM)	Linear SVM	LOOCV	First sample, 80.0%; Second sample, 59.0%	L. IPL, bilateral FG	Predetermined ROIs. Independent
Zare et al. (2016)	Familial risk of dyslexia	24 (12 with familial risk, 12 without risk)	0.5	rest-EEG (FC)	SVM (linear and 3 nonlinear kernels)	LOOCV	79.2% (linear and cubic)	Left frontal and bilateral parietal channels	Predetermined channels. Non- independent
Płoński et al. (2017)	Dyslexia	236 (130 dyslexia, 106 TD)	8.5-13.7	sMRI (volume, cortical thickness, surface area, folding index, and mean curvature)	Linear SVM, Logistic regression, RF	LOOCV and repeated 10-fold CV (100 times)	65.0%	L. MTG, L. STG, L. frontal pole, L. precuneus	CV within training data
Cui et al. (2018)	Reading scores, Dyslexia	First sample, 507; second sample, 372; third sample, 67(25 dyslexia, 42 TD)	First sample, 22-35; second sample, 22- 35; third sample, 11.0	sMRI (GM)	Elastic net	3-fold CV	First sample, $r =$ 0.43; second sample, $r =$ 0.34; third sample, $r =$ 0.24	Large portions of the frontal, temporal, parietal, occipital cortices, subcortex and cerebellum	Weight values
Dimitriadi s et al. (2018)	Dyslexia	52 (25 dyslexia, 27 TD)	Dyslexia, 12.2; TD, 11.4	rest-MEG	kNN, SVM	Repeated 5-fold CV (100 times)	97.0%	Parietal and temporal channels	Correlation between weight values and behavioral scores

Table 1. Cross-sectional prediction studies for literacy

Zainuddi n et al. (2018)	Dyslexia	33 (17 poor dyslexia, 8 capable dyslexia, 8 TD)	7-12	task-EEG (word comprehensi on)	Nonlinear SVM	10-fold CV	91.0%	No specific information	N.A.
Barranco - Gutiérrez (2020)	L2 speakers and natives	19 L2 English speakers and 25 natives	L2 speakers, 31.9; natives 28.2	dMRI	ANN	75% for training, 10% for validation, 15% for testing	97.0%	Corpus callosum	Predetermined ROIs. Independent
Cignetti et al. (2020)	Dyslexia, DCD	136 (45 dyslexia, 20 DCD, 29 comorbid, 42 TD)	Dyslexia, 10.2; DCD, 10.0; comorbid, 10.2; TD, 10.1	rest-fMRI (FC)	Linear SVM	LOOCV	75.9% (comorbid vs. TD)	Default mode, dorsal attention, ventral attention, frontoparietal networks	Weight values
Kristanto et al. (2020)	Reading scores	998	22-35	sMRI (thickness, myelination, sulcus depth), rest- fMRI (FC), dMRI (connectivity strength)	Linear regression	2-fold CV with LOOCV in each fold	r = 0.21	Large portions of the frontal, temporal, and parietal cortices	CV within training data
Lei et al. (2020)	Second language proficiency	40 native Japanese (20 high- and 20 low- proficiency), 38 native English speakers (19 high- and 19 low- proficiency)	Japanese, high, 28.1; low, 29.4; English, high, 29.3; low, 28.5	task-fNIRS	Linear SVM, kNN, Sparse logistic regression	LOOCV	81.9% (English, SVM)	L. MFG, L. PreCG, L. ITG, L. PostCG, L. AG, bilateral STG, bilateral MTG	Sparse canonical correlation analysis
Tomasi & Volkow (2020)	Reading and vocabulary scores	424	29.0	rest-fMRI (FC), task- fMRI (language, working memory, and motor tasks, FC)	Linear regression	2-fold CV with LOOCV in each fold	R = 0.33	Fronto-parietal and default mode networks	CV within training data
Zahia et al. (2020)	Dyslexia	55 (19 dyslexia, 17 monocular vision, 19 TD)	Dyslexia, 10.5; monocular vision, 10.4; TD, 10.0	task-fMRI (lexical decision, orthographic matching, semantic categorizatio n)	ANN (3D CNN)	4-fold CV	72.3%	Bilateral IFG, MTG, STG, precuneus, FG, L. AG, L. medial temporal	Predetermined ROIs. Independent
Formoso et al. (2021)	Dyslexia	48 (16 dyslexia, 32 TD)	Dyslexia, 8.0; TD, 7.8	task-EEG (auditory stimuli listening)	NBC	5-fold CV	90.0% (Beta, 16Hz)	Alpha, beta, delta, theta, gamma bands	N.A.
Mascher etti et al. (2021)	Dyslexia	44 (22 dyslexia, 22 TD)	Dyslexia, 14.1; TD, 13.2	task-fMRI (visual detection)	Multiple kernel learning SVM	10-fold CV	65.9%	11 ROIs including R. SPL, L. IPL, R. IFG, and occipital cortex	Weight values
McNorga n (2021)	High-skilled and poor readers	First sample, 28 (14 high- skilled and 14 poor readers); second sample, 10 (5 high-skilled and 5 poor readers)	First sample, 8-13; second sample, 8-14	task-fMRI (rhyme judgment, multiplication , FC)	ANN (MLP)	10-fold CV, 3- fold CV	First sample, 94.0%; second sample, 96.0% (of functional connectivity)	115 ROIs across the brain	Predetermined ROIs. Non-independent

Tomaz Dyslexia Da Silva	32 (16 dyslexia, 16	Dyslexia, 9.6; TD, 8.4	task-fMRI (word	four ANNs (grammar-	80% for training, 10% for	94.8% (GGP 2D CCN)	Large portions of the frontal, parietal.	Weight values
et al. (2021)	TD)		reading)	based genetic programming [GGP] CNN, GGP 3D CNN, LeNet- 5, LeNet-5 3D), linear SVM	validation, 10% for testing	,	temporal and occipital cortices	
Usman Dyslexia et al. (2021)	Dyslexia, 91; TD, 57	Dyslexia, 11.4; TD, 19- 30	sMRI (GM), task-fMRI (rhyming, spelling, semantic decision), rest-fMRI, dMRI	ANN (two- ways cascaded CNN, ResNet-50, Inception V3)	Repeated 10-fold CV (10 times)	94.7% (ResNet50)	L. STG, L. OTG, lateral cerebellum	Predetermined ROIs. Independent
Yu et al. Familial risk o (2022) dyslexia	f 98 (35 with familial risk, 63 without risk)	Risk, 8.9; without risk, 8.3	rest-fMRI (FC)	Linear SVM	LPOCV	55.0%	L. FG	Predetermined ROIs. Non-independent. Weight values
Joshi et Dyslexia al. (2023)	192 (96 dyslexia, 96 TD)	Dyslexia, 9.9; TD, 9.8	sMRI (GM, WM)	ANN (autoencoder), SVM, RF	Repeated sampling (100 times) with 80% for training, 20% for testing	75.0% (ANN)	L. IPL, R. orbitofrontal, L. STG	Classification accuracy with image perturbation
Nemmi Dyslexia, DCI et al. (2023)	0 136 (45 dyslexia, 20 DCD, 29 comorbid, 42 TD)	Dyslexia, 10.2; DCD, 1.0; comorbid, 10.2; TD, 10.1	sMRI (GM, WM), rest- fMRI (ALFF, local and global correlation)	RF, linear SVM	Repeated 10-fold CV (10 times)	Dyslexia, 79.0%; DCD, 58.0%; comorbid, 62.0% (SVM)	12 ROIs including L. cerebellum, R. MFG, R. SFG, R. LOC, L. insula, R. putamen, R. insula, and R. STG	Predetermined ROIs. Non-independent
Yuan etReading andal.vocabulary(2023)scores	522	28.5	rest-fMRI (FC)	Relevance vector regression	LOOCV	Reading test, <i>r</i> = 0.25; vocabulary test, <i>r</i> = 0.29	4 networks across frontal and temporal cortices	Predetermined ROIs. Independent
Zhang et Second al. language (2023) proficiency	47 (15 low-, 16 moderate-, 16 high-	22.7	task-fMRI (story listening)	SVM, Ridge regression	LOOCV	49.0%, <i>r</i> = 0.47	Large portions of the frontal, parietal, temporal and	Predetermined ROIs. Non-independent

248 typically-developing; dMRI, diffusion magnetic resonance imaging; fMRI, functional MRI; sMRI, 249 structural MRI; EEG, electroencephalography; MEG, magnetoencephalography; fNIRS, 250 functional near-infrared spectroscopy; GM, gray matter; WM, white matter; ALFF, amplitude of low-frequency fluctuations; FC, functional connectivity; LOOCV, leave-one-out cross-validation; 251 252LPOCV, leave-pair-out cross-validation; ROI, region-of-interest; AG, angular gyrus; FG, fusiform 253 gyrus; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; ITG, inferior temporal gyrus; LOC, lateral occipital cortex; MFG, middle frontal gyrus; MTG, middle temporal gyrus; PreCG, 254255 precentral gyrus; PostCG, postcentral gyrus; SFG, superior frontal gyrus; SMG, supramarginal 256 gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus.

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In comparison to the number of studies that have used cross-sectional

designs to predict literacy outcomes, a much smaller number of studies have

260 used longitudinal designs to make out-of-sample predictions of literacy

outcomes (**Table 2**). A pioneering study by Hoeft et al. (2007) combined both

task-fMRI (rhyme judgment) and sMRI (GM and WM) data as inputs of multiple

²⁶³ linear regression models. The authors found that brain data could predict later

reading scores at the end of the same year. Bach et al. (2013) combined task-

265 EEG and task-fMRI data (word comprehension) to predict reading scores 266 measured 2 years later. In Feng et al. (2021), subjects underwent grammar 267 training of an artificial language. Their final learning outcomes were predicted 268 from task-fMRI data during training in earlier sessions. Beyer et al. (2022) used 269 sMRI data (GM, surface area, and local dyrification) in preschoolers to predict 270 literacy ability 2 years later. This study is particularly interesting because 271 children were tested before they were exposed to formal education. This finding 272 lends support to the argument that neuroimaging measures may be used as a 273 way to improve the early detection of learning difficulty, in order to prevent 274 difficulties later on (Mascheretti et al., 2017).

275 Some longitudinal neuroimaging studies have also attempted to use 276 neural data to classify between children with and without dyslexia. For example, 277 Hoeft et al. (2011) showed that a machine-learning classifier can distinguish whether certain dyslexic children will improve their reading skills or not 2.5 278 279 years later using fractional anisotropy (FA) of dMRI and task-fMRI (rhyme 280 judgment) data. Skeide et al. (2016) also reported successful classification of future dyslexia based on sMRI (GM) data in children before formal education. 281 Finally, Yu et al. (2020) demonstrated classification of children with and without 282 283 familial risk of dyslexia using task-fMRI data (phonological processing) before formal education. These reports suggest that prediction of language ability 284 285 before formal education may be applicable to the early detection of risk of 286 language deficits. In sum, both cross-sectional and longitudinal designs suggest 287 that neuroimaging data may have the potential to predict literacy skills and 288 classify language disorders. 289

Data type Max prediction Study Target Sample size Mean Technique Cross-Brain areas Selection validation method of brain ability/grou age/age accuracy areas ps range task-fMRI Reading LOOCV R. FG, L. MTG, R. Hoeft et 64 T1: 10.0, T2: Multiple linear Unclear Predetermined scores after 10.6 (rhyme regression MFG, L. STG, L. IPL ROIs. Nonal (2007) one school judgment), independent vear sMRI (GM, WM) LOOCV Hoeft et Improvement 25 (12 T1: with gain task-fMRI Linear SVM 92.0% Whole brain, R. IFG, Predetermined al. (2011 of reading dysÌexia with 14.5; without (rhyme R. SLF ROIs. judgment), Independent gain, 13 gain, 14.6; scores in dyslexia afte without gain T2: with gair dMRI (FA) 17.0; without 2.5 years gain, 16.0 19 T1: 6.4, T2: DA LOOCV Bach et Reading task-EEG. 94.1% L. FG, L. occipito-Predetermined 8.4 scores after task-fMRI temporal channels ROIs. al. Independent (2013) 2 vears (word

290	Table 2. Longitudina	al prediction	studies fo	r literacy
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				comprehensio n)					
				,					
Skeide et al. (2016)	Dyslexia after 1.7 years and at the end of the first grade	First sample: 34 (17 dyslexia, 17 TD); second sample 20 (10 dyslexia, 10 TD)	T1: First sample, dyslexia, 10.4; TD, 10.6; second sample, dyslexia, 5.6; TD, 5.8; T2: unclear	sMRI (GM, WM)	Linear SVM	10-fold CV	First sample: 73.5%; second sample: 75.0%	L. FG	Prediction accuracy, predetermined ROIs. Non- independent
Yu et al. (2020)	Familial risk of dyslexia	81 (35 with risk, 34 without risk, 12 dyslexia and with familial risk)	T1: with risk, 5.5; without risk, 5.4; dyslexia, 5.8; T2: with risk, 8.7; without risk, 9.0; dyslexia, 8.3	task-fMRI (phonological processing)	Linear SVM	15-fold CV	68.3%	R. IFG, L. AG	Searchlight
Feng et al. (2021)	Learning outcomes after 7 days training in an artificial language	33	T1/T2: 22.3	task-fMRI (vocabulary and grammar training)	Least-squares SVR	Repeated 10- fold CV (10000 times)	<i>r</i> = 0.61	23 ROIs across frontoparietal, perisylvian, salience, and default mode networks	Weight values
Beyer et al. (2022)	Literacy skill after 2 years	42	T1: 5.6, T2: 8.3	sMRI (GM, surface area, local gyrification)	Elastic net	LOOCV, repeated 10-fold CV (50 times)	r = 0.80	L. IFG, STG, MTG, insula, ITG, FG, SMG, AG	Predetermined ROIs. Independent. Weight values

291 SLF, superior longitudinal fasciculus.

292

293 Can neuroimaging studies predict numeracy skills?

As is the case for studies on literacy, neuroimaging studies that attempt to predict numeracy skills can be categorized as either cross-sectional (**Table 3**) or longitudinal (**Table 4**). Cross-sectional studies include for example Ullman & Klingberg (2017), who estimated math scores of 6- to 7-year-olds through a prediction model of brain age using dMRI (FA). Pina et al. (2022) predicted four types of math scores (math fluency, calculation, applied problems, quantitative concepts) using 100 radiomics features derived from sMRI data.

301 Other cross-sectional studies have attempted to classify groups of 302 participants with respect to their numeracy skills, for example those with and 303 without dyscalculia. Dyscalculia is defined as a specific learning difficulty in 304 processing numerical information, learning arithmetic facts, and performing

- 305 calculations, with otherwise normal intelligence (American Psychiatric
- Association et al., 2013). For example, Rykhlevskaia et al. (2009), Jolles et al.
- 307 (2016), and Dinkel et al. (2013) showed that children with and without
- 308 dyscalculia could be classified using dMRI (number of pathways), rest-fMRI
- 309 (FC), and task-fMRI data (dots comparison and calculation), respectively.
- 310 Moreover, Mórocz et al. (2012) and Peters et al. (2018) showed that arithmetic

- 311 task-fMRI data can be used to classify both dyscalculic and dyslexic children.
- 312 Torres-Ramos et al. (2020) also showed that task-EEG data (digits comparison)
- 313 could be used to classify children according to three different categorical levels
- of math achievement.

Several studies have focused on classifying other aspects of individual differences in numeracy skills. Shim et al. (2021) and Liu et al. (2022) reported classification of individuals based on their expertise in mathematics using restfMRI (FC) and sMRI data, respectively. Ventura-Campos et al. (2022) classified individuals who make errors in variable selection (reversal error) when writing equations to given word problems using algebra task-fMRI data.

321

Study	Target ability/gro ups	Sample size	Mean age/age range	Data type	Technique	Cross- validation	Max prediction accuracy	Brain areas	Selection method of brain areas
Rykhlevs kaia et al. (2009)	Dyscalculia	47 (23 dyscalculia, 24 TD)	Dyscalculia, 8.8; TD, 8.9	dMRI (number of pathways)	SVM	10-fold CV	70.0%	58 ROIs located in the posterior part of the brain	Predetermined ROIs. Independent
Mórocz et al. (2012)	Dyscalculia and dyslexia	58 (36 control, 13 dyscalculia, 9 dyslexia)	TD, 25.6; Dyscalculia, 22.5; dyslexia, 24.6	task-fMRI (multiplication)	Nonlinear SVM	LOOCV	Unclear	24 ROIs across frontal, parietal, temporal, occipital cortices, and cerebellum	Predetermined ROIs. Independent
Dinkel et al. (2013)	Dyscalculia	32 (16 dyscalculia, 16 TD)	Dyscalculia, 8.2; TD, 8.2	task-fMRI (dots comparison and calculation)	Linear SVM	LOOCV	87.5% (dot comparison)	Bilateral IPS, L. thalamus, R. paracentral lobule, R. frontal operculum, R. cingulate gyrus	Predetermined ROIs. Independent
Jolles et al. (2016)	Dyscalculia	38 (19 dyscalculia, 19 TD)	Dyscalculia, 8.9; TD, 8.8	rest-fMRI (FC)	Linear SVM	LOOCV	L. IPS, 84.2%; R. IPS, 76.3%	Bilateral IPS	Predetermined ROIs. Independent
Ullman & Klingber g (2017)	Math and working memory scores	First sample, 82; second sample, 31	First sample, 6- 20; second sample, 6.8	dMRI (FA)	Linear SVR	LOOCV	Working memory, <i>r</i> = 0.50; math, <i>r</i> = 0.41	No specific information	N.A.
Peters et al. (2018)	Dyscalculia and dyslexia	52 (14 dyslexia, 8 dyscalculia, 8 comorbid, 22 TD)	10.8	task-fMRI (subtraction)	Unclear	Repeated LPOCV (Leave- pair-out CV, 1000 times)	Unclear	Frontal, parietal, temporal, and occipital cortices	Predetermined ROIs. Independent
Torres- Ramos et al. (2020)	Math achieveme nt level	57 (18 High, 20 average, 19 low achievements)	High, 8.6-9.9; average, 8.2-9.9; low, 8.3-10.8	task-EEG (digits comparison, FC)	Decision trees	10-fold CV	80.0% (alpha band)	Alpha, beta, delta, theta bands	N.A.
Shim et al. (2021)	Mathemati cian and non- mathemati cians	44 (21 mathematician s, 23 non- mathematician s)	Mathematicians, 33.4; non- mathematicians 27.2	rest-fMRI (FC)	SVM	LOOCV	90.9% (with 39 connection features)	46 pairs of ROIs across the brain	Predetermined ROIs. Non- independent

322 **Table 3. Cross-sectional prediction studies for numeracy**

Liu et al. (2022)	Math and non-math students	123 (72 math, 51 non-math)	Unclear	sMRI	ANN (MLP and ResNet)	5-fold CV	91.8%	L. MFG	Predetermined ROI. Independent
Pina et al. (2022)	Math scores	77	9.7	sMRI (100 radiomics features)	RF regression	Repeated 5-fold CV (20 times)	Unclear	15 regions across frontal and parietal cortices	Prediction accuracy
Ventura- Campos et al. (2022)	Groups with reversal error or not using algebraic problems	20 (10 reversal error, 10 without error)	Reversal error, 21.3; without error, 21.7	task-fMRI (algebra)	13 methods (DA, ANN, SVM, RF, kNN)	LOOCV	80.0% (flexible DA)	8 ROIs across frontal and parietal cortices	Predetermined ROIs. Non- independent

323 IPS, intraparietal sulcus.

324

325 In contrast to what has been done in studies focusing on literacy, a 326 greater number of studies have used a longitudinal design to predict numeracy 327 skills (Table 4). In a seminal study relying on multivariate regression, Supekar et al. (2013) showed that sMRI (GM) and rest-fMRI (FC) data could predict 328 329 improvements in math performance of 8-year-old children after 8 weeks of 330 tutoring program consisting of conceptual instruction and speeded arithmetic 331 fact retrieval. Evans et al. (2015) further showed that prediction of longitudinal 332 math outcome is possible even 6 years later using sMRI (GM) and rest-fMRI 333 data. Chang et al. (2022) also reported similar prediction of change in 334 performance after 4 weeks of training using rest-fMRI (FC) data. Schwartz et al. 335 (2020) used fMRI data during a transitive reasoning task to predict math 336 calculation skills 1.5 years later. Ullman et al. (2015) showed that math and 337 working memory scores could be predicted at ages 5 and 7 from neonatal dMRI 338 (FA), but not from sMRI data. Therefore, studies show that numeracy skills may 339 be predicted from brain activity associated with domain-general processing, 340 consistent with the role of these processes in math learning (Raghubar et al., 341 2010).

342 We found only one longitudinal neuroimaging study that focused on the 343 classification of dyscalculia as is depicted in Figure 1. Kuhl et al. (2021) 344 classified future dyscalculia at ages of 7-9 and typically-developing (TD) 345 children based on dMRI and rest-fMRI data before formal education (at ages of 346 3-6). Overall, similar to language abilities, studies show that neuroimaging data 347 may have the potential to predict numeracy skills and classify their disorders. 348 Note that some longitudinal studies do not neatly fall into the categories 349 described in Figure 1. For example, Qin et al. (2014) used differences between

addition task-fMRI data from two time points (T1 and T2, 1.2 years later) to

351 predict improvements in the frequency of retrieval strategy for addition problem 352 solving. luculano et al. (2015) showed that task-fMRI data (mental addition) can discriminate between children with and without dyscalculia before (but not after) 353 354 8 weeks of a tutoring program involving conceptual instruction and speeded 355 arithmetic fact retrieval training. Michels et al. (2018) also reported similar 356 results based on 5 weeks of mental number line training. These studies represent different ways to combine machine learning with neuroimaging data

- 357
- 358 to explain differences in numeracy skills.

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Study	Target ability/groups	Sample size	Mean age/age range	Data type	Technique	Cross- validation	Max prediction accuracy	Brain areas	Selection method of brain areas
Supekar et al. (2013)	Improvements in math scores after 8 weeks of training	40 (24 with training, 16 control)	T1/T2: with training, 8.5; control, 9.0	sMRI (GM), rest-fMRI (FC)	Linear regression	4-fold CV	r = 0.45	R. hippocampus	Predetermined ROIs. Independent
Qin et al. (2014)	Improvements in the frequency of retrieval-strategy use 1.2 years later	28	T1: 8.3, T2: 9.5	task-fMRI (addition, FC)	Linear regression	4-fold CV	<i>r</i> = 0.71	R. hippocampus, L. IPS, bilateral DLPFC	Predetermined ROIs. Non-independent
Evans et al. (2015)	Math scores up to 6 years later	43	T1: 8.7, T2: unclear	rest-fMRI, sMRI (GM)	Linear SVR	4-fold CV	R ² = 0.44	L. FG, L. IPS, L. DLPFC, L. VLPFC, R. premotor cortex, R. cuneus	Predetermined ROIs. Non-independent
luculan o et al. (2015)	Dyscalculia after 8 weeks of training	30 (15 dyscalculia, 15 TD)	T1/T2: Dyscalculia, 8.7; TD, 8.5	task-fMRI (addition)	Linear SVM	LOOCV	Before training, 83.3%; after training, 43.3%	17 ROIs across frontal, parietal, temporal cortices, subcortex, and cerebellum	Predetermined ROIs. Non-independent
Ullman et al. (2015)	Math and working memory scores after 5 and 7 years	272 (224 preterm infants, 46 control)	T1: 40.3 weeks (gestational age), T2: unclear	sMRI (deformatio n-based morphomet ry), dMRI (FA)	SVR	LOOCV	r = 0.36 at 5 years	No specific information	N.A.
Michels et al. (2018)	Dyscalculia after 5 weeks training	31 (15 dyscalculia, 16 TD)	T1/T2: 9.5	task-fMRI (number order judgment)	Unclear	LOOCV	Before training, 86.4%; after training, 38.9%	Unclear	Predetermined ROIs. Non-independent
Schwart z et al. (2020)	Math scores 1.5 years later	31	T1: 11.0, T2: 12.6	task-fMRI (reasoning)	Kernel ridge regression	LOOCV	r = 0.39	R. IPS	Predetermined ROIs. Non-independent
Kuhl et al. (2021)	Dyscalculia	30 (15 dyscalculia, 15 TD)	T1: Dyscalculia, 4.1; TD, 5.0; T2: 7-9	rest-fMRI (ALFF, regional homogeneit y, degree centrality), dMRI (streamline density)	SVM	10-fold CV	86.7%	R. IPS, R. DLPFC	Searchlight
Chang et al. (2022)	Improvements in math scores after 4 weeks of training	52 (18 dyscalculia, 34 TD)	T1/T2: 8.2	rest-fMRI (FC)	Linear regression	4-fold CV	r = 0.33	Bilateral hippocampus, L. IPS	Predetermined ROIs. Non-independent

360 Table 4. Longitudinal prediction studies for numeracy

361 DLPFC, dorsolateral prefrontal cortex; VLPFC, ventrolateral prefrontal cortex.

363 Can neuroimaging studies predict other skills relevant to academic364 achievement?

365 In our review of studies above, we exclusively focused on studies that have 366 examined literacy and numeracy skills. However, studies have also tested 367 whether neuroimaging may predict other skills that are relevant to academic 368 achievement. This is notably the case for vocal communication. For example, 369 Abrams et al. (2016) used task-fMRI data from 10-year-olds listening to their 370 mother's voice to predict children's communication scores. This is also the case 371 for affective traits related to academic achievement, particularly numeracy skills. 372 Young et al. (2012), for example, classified children with high and low math 373 anxiety groups using task-fMRI (addition and subtraction). Chen et al. (2018) 374 predicted individual differences in positive attitudes toward mathematics using 375 right hippocampal activity during an addition task. Supekar et al. (2015) showed 376 that activity changes in task-fMRI during addition task can predict changes in 377 children's math anxiety elicited by the same tutoring program. Finally, studies have attempted to use brain information to enhance the diagnosis of autism 378 379 spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (Eslami et 380 al., 2020; Nogay & Adeli, 2020), both of which can have impact on academic 381 achievement (Arnold et al., 2020; Whitby & Mancil, 2009). luculano et al. (2014) 382 notably used task-fMRI data (mental addition) to classify between ASD and TD 383 children, suggesting a potential relation between the autistic trait and numeracy 384 skills. While these developmental disorders are beyond the scope of this paper, 385 they are important targets that cannot be ignored when considering the overall 386 application of neuroimaging and machine learning to education.

387 In addition to predicting literacy and numeracy skills, studies have also 388 used brain imaging data to predict academic achievement more generally. For 389 example, Wang et al. (2019) predicted students' academic achievement at ages 390 17-20 using sMRI data. Rasheed et al. (2021) predicted academic achievement 391 (math and language test scores) of school children 4 years later using EEG 392 data. Maglanoc et al. (2020) used a large sample of rest-fMRI data from the UK 393 Biobank to predict educational attainment (based on the gualification variables, 394 e.g., university degree). Studies have also investigated to what extent domain-395 general skills contributing to academic achievement may be predicted using 396 neuroimaging, including working memory, attention, and intelligence. For

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397 example, Ullman et al. (2014) used sMRI and task-fMRI during a visuospatial 398 working memory task to predict children's working memory capacity 2 years 399 later. There are also a large number of studies on the prediction of intelligence 400 quotient scores from brain data (see Vieira et al. (2022) for a recent systematic 401 review). For example, Greene et al. (2018) used both rest- and task-fMRI data 402 with working memory and emotion identification tasks and found that task-fMRI 403 models outperformed rest-fMRI model in predicting fluid intelligence scores. 404 Therefore, a number of studies provide evidence that neuroimaging may predict 405 general cognitive functioning, though this may not be as relevant as the 406 prediction of specific academic skills such as reading or math for the purpose of 407 identifying children with specific learning difficulties.

408

409 Are there any specific brain circuits supporting prediction of academic410 outcomes?

The studies reviewed here are important not only for practical reasons (i.e., to predict outcomes), but also for understanding the brain mechanisms supporting literacy and numeracy acquisition. **Tables 1-4** report the main brain regions that have been identified in the specific studies.

415 Some consistency can be seen across studies. For example, studies 416 that have used MRI data to classify participants with and without dyslexia have 417 often identified the left fusiform gyrus (FG) (Skeide et al., 2016; Tamboer et al., 418 2016; Yu et al., 2022; Zahia et al., 2020), and the left superior temporal gyrus 419 (STG) (Joshi et al., 2023; Płoński et al., 2017; Usman et al., 2021; Zahia et al., 420 2020) as a potential neuromarker of the condition (see Table S1 for a list of 421 studies only focusing on dyslexia). Studies that have used MRI data to classify 422 participants with and without dyscalculia have instead often identified the right 423 intraparietal sulcus (IPS) (Dinkel et al., 2013; Jolles et al., 2016; Kuhl et al., 424 2021) (see **Table S2** for a list of studies only focusing on dyscalculia). Although 425 the number of studies remains too limited to guantify the consistency of these 426 findings in a meta-analysis, these findings suggest that these specific brain 427 circuits may be important for academic learning and be the target of future 428 studies.

However, as can also be seen from the tables, the brain systems identified between studies are wide and span the frontal, temporal, parietal, and occipital cortices, as well as subcortical areas. To some extent, this variability is expected given the different domains (e.g., literacy vs, numeracy), brain 433 measures (e.g., EEG, fMRI, sMRI) and tasks (e.g., addition vs. reasoning) 434 explored between studies. Another factor contributing to such variance may be 435 the use of different tests to estimate math and reading scores, and inconsistent 436 definitions of conditions such as dyscalculia and dyslexia. For example, while 437 some studies (e.g., Jolles et al., 2016) considered children with dyscalculia as having at or below the 25th percentile using standardized math test scores, 438 others (e.g., Dinkel et al., 2013) have used more stringent criteria and focused 439 on children having at or below the 10th percentile. In other words, variability in 440 441 findings is expected given the wide variability in methods between studies. In 442 what follows, we will argue that some critical differences in both machine 443 learning algorithms and cross-validation methods used between studies might 444 also underlie some of this variability.

445

446 Studies use a range of machine learning methods

447 As shown in Figure 1, neuroimaging studies predicting academic outcomes can 448 be classified as belonging to one of the four categories. However, studies 449 largely differ with respect to the specific machine learning algorithms they rely 450 on to predict behavior, which is the first important source of variability in the 451 literature. Many classification studies have used linear support vector machine 452 (SVM) (Tables 1-4). Briefly, SVM is a supervised classification algorithm that 453 constructs a set of hyperplanes separating given classes in a high dimensional 454 space, so as to maximize the distance between the nearest data points of any 455 class (Cortes & Vapnik, 1995). The SVM, which is implemented in several 456 decoding toolboxes as a default method (e.g., The Decoding Toolbox; Hebart et 457 al., 2014), is useful for classifying among different groups, such as children with 458 learning disability versus controls. However, studies have also used other 459 techniques, such as logistic regressions (Cui et al., 2016), decision trees (Torres-Ramos et al., 2020), random forest (RF) (Nemmi et al., 2023), naïve 460 461 Bayes classifiers (NBC) (Formoso et al., 2021), discriminant analysis (DA) 462 (Bach et al., 2013), k-nearest neighbors (kNN) (Ventura-Campos et al., 2022), 463 and artificial neural networks (ANN) (Tomaz Da Silva et al., 2021).

A number of different machine learning methods have also been used in
regression studies, though there is more homogeneity among these studies
than among classification studies. For instance, some studies have used linear
regression, while others have used support vector regression (SVR) (He et al.,
2013), relevance vector regression (Yuan et al., 2023), kernel ridge regression

469 (Schwartz et al., 2020), and elastic net (Beyer et al., 2022). Simple or multiple 470 linear regression requires a reduction of input data into a limited number of 471 variables, which has been achieved by focusing on predetermined regions of 472 interest (Hoeft et al., 2007; Supekar et al., 2013) or connectivity among them 473 (Chang et al., 2022). However, inclusion of too many parameters can cause 474 models to overfit the training data that contains non-negligible amount of noise, 475 resulting in reduced generalizability to test data (Bishop, 2006). Elastic net and 476 other regularized regression methods implement constraints on the model 477 weight values to minimize overfitting to the training data and are appropriate for 478 high-dimensional brain data. More recently, connectome-based predictive 479 modeling (CPM) based on linear regression has been adopted for the analysis 480 of brain-behavior association (Shen et al., 2017). For example, researchers 481 have used this technique to analyze the HCP dataset, which includes a large 482 number of subjects (Kristanto et al., 2020; Tomasi & Volkow, 2020).

483 Although the use of different algorithms is in itself not problematic, it 484 may become so when no justification is given for using one method instead of another. This is unfortunately often the case in the literature. This 485 486 methodological flexibility increases the researcher degrees of freedom and 487 makes it difficult to parse out exploratory from confirmatory findings, especially given an absence of preregistration across studies (Poldrack et al., 2017). 488 489 There is also a need for more direct comparison between methodologies. For 490 instance, Płoński et al. (2017) tested SVM, logistic regression, and RF for the 491 same dataset, and reported that logistic regression showed the highest 492 classification accuracy for dyslexia. Furthermore, Ventura-Campos et al. (2022) 493 compared 13 different classification methods and reported that flexible 494 discriminant analysis outperformed other methods. This type of systematic 495 approach can ensure the robustness of results independent of the analysis 496 method. However, this also requires researchers to systematically adopt the 497 most robust methods, which might not always be the case. For example, a 498 meta-analysis on machine learning application for disease prediction reported 499 that SVM is the most frequently used algorithm in the literature, while RF shows 500 superior accuracy (Uddin et al., 2019). By comparing six regression methods, 501 Cui & Gong (2018) reported that least absolute shrinkage and selection 502 operator (LASSO) regression were worse than the other algorithms when using 503 FC of rest-fMRI data, while ordinary least-square regression was worse when 504 using the sum of FC from each brain region, suggesting that performance of

different algorithms also depends on preprocessing methods of the same brain
 data. To our knowledge, it remains unclear which method is more effective for
 predicting academic achievement.

508 Another source of variability in machine learning methods is the cross-509 validation (CV) method employed (e.g., split-half, 10-folds, leave-one-out). CV is 510 a widely-known method in machine learning to iteratively split some data into 511 training and test samples, testing the model generalizability while minimizing 512 selection bias. In the case of k-fold CV, 1/k of the original data are selected as 513 test samples in each iteration and this procedure covers all original data with k 514 iterations. In contrast, leave-one-out CV (LOOCV) uses each individual data 515 (e.g., subject) as a test sample and iterates across all data. Among the studies 516 included in the current review, LOOCV was the most widely adopted (23 517 studies), while other studies used various types of k-fold CV methods (10-fold CV, 8 studies; 4-fold CV, 6 studies). Recent studies suggested that the 518 519 repeated random splits method is more reliable than the leave-one-out method 520 (Valente et al., 2021; Varoquaux et al., 2017). In this method, CV based on 521 different random sample splitting is repeated for multiple times and averaged 522 (e.g., 100 times); 10 studies adopted this technique (Beyer et al., 2022; Nemmi 523 et al., 2023). Overall, there is wide variability in the machine-learning techniques 524 used in neuroimaging studies, both in terms of algorithm selection and CV 525 method. Both of these may have substantial influence on the model 526 performance. This calls for a standardization in the field and future research 527 would require careful consideration of their methodological choices. 528

529 Limitations and future directions

As reviewed here, an increasing number of neuroimaging studies suggest that brain data can be used to predict individual differences in both literacy and numeracy skills, as well as other skills relevant for academic achievement.

533 However, several limitations are apparent in the literature.

534 First, the majority of articles reviewed here have used sMRI or resting 535 fMRI data (**Tables 1-4**). Although some studies have used task-fMRI data, their 536 sample size was also generally smaller than sMRI and rest-fMRI studies. 537 However, task-fMRI data can contribute to more accurate prediction of 538 individual differences in academic achievement. For example, a recent study 539 has reported superiority of movie-watching task-fMRI data in predicting various cognitive and emotional traits compared to rest-fMRI data (Finn & Bandettini,
2021; Greene et al., 2018). Combining multiple task-fMRI data may further
increase prediction performance (Hammer et al., 2015). Moreover, task-fMRI
can shed light on the heterogenous profiles of children with dyscalculia or
dyslexia, who might have specific difficulties in some cognitive skills (such as
phonological or visual attentional deficits in the case of dyslexia) by targeting
appropriate ROIs (Jednoróg et al., 2014; van Ermingen-Marbach et al., 2013).

547 Second, the literature is largely dominated by MRI data and relatively 548 few studies have used EEG, MEG, or fNIRS in predictive studies. For instance, 549 to the best of our knowledge, Dimitriadis et al. (2018) was the only example of 550 using MEG data to predict language disorders. Lei et al. (2020) was also the 551 only example of using fNIRS data to predict second language proficiency. The 552 wide usage of MRI data might be due to its advantage in spatial resolution 553 compared to the other methods. Considering their portability, however, EEG, 554 fNIRS, and optically pumped magnetometers (OPM)-MEG (Boto et al., 2018; 555 Brookes et al., 2022), as well as portable MRI (Liu et al., 2021), are interesting because they are more accessible for experimentation in schools and clinical 556 557 practices than conventional MRI (Stangl et al., 2023). Given that early detection 558 of potential learning disabilities is an important goal of several neuroimaging 559 studies discussed here (Hoeft et al., 2007), efforts should be made to evaluate 560 the potential of task-related portable neuroimaging data for predicting outcomes in children. 561

562 Third, most previous studies recruited subjects who were already 563 exposed to formal education. However, predicting outcomes from neuroimaging 564 data may be most interesting before potential difficulties occur at the behavioral 565 level. That is, brain data might help detect a risk for learning disabilities before 566 children begin formal education, which may help ensure that children receive 567 appropriate educational support at the earliest stage. To our knowledge, four 568 studies in the literacy domain (Beyer et al., 2022; Skeide et al., 2016; Yu et al., 569 2020; Zare et al., 2016) and two studies in the numeracy domain (Kuhl et al., 570 2021; Ullman et al., 2015) tested children before the onset of formal education. 571 Most of these studies used either sMRI or rest-fMRI, and only one study used 572 task-fMRI data (Yu et al., 2020). The relative lack of studies might reflect the 573 inherent difficulty of pediatric MRI with young children. Again, this calls for the 574 use of more child-friendly portable measurement techniques to inform about the 575 prediction of future academic outcomes.

576 Fourth, there is still room for the integration of sophisticated machine 577 learning methods. Although linear regression and SVM are the two most widely 578 used techniques in previous studies, some recent studies have adopted ANNs 579 (Joshi et al., 2023; Tomaz Da Silva et al., 2021; Zahia et al., 2020). ANN is a 580 computational model inspired by biological neural networks (BNNs). It consists 581 of multiple layers of neuronal units, where the weighted sum of units in one 582 layer is used as input for the next layer after a nonlinear transformation. One 583 advantage of using ANNs is that one can compare commonality between ANNs 584 and BNNs in terms of their representations across different layers/regions 585 (Goldstein et al., 2022; Nakai & Nishimoto, 2023; Schrimpf et al., 2021). 586 However, it remains unclear which ANN model is the more appropriate to 587 explain developmental changes in brain representations and differences 588 between those with and those without learning disabilities. Cross-validation 589 techniques might also be improved. Although the large majority of studies use 590 left-out sample predictions, this method is not the only method for brain-based 591 classification or regression. Siegelman et al. (2021), for example, recently 592 proposed a Bayesian latent-mixture model framework to classify between 593 children with and without dyslexia. This framework does not need left-out 594 samples because it constructs classification models by only using neuroimaging 595 data without any categorical labels. In other words, it interprets the fit between 596 the models' classification and categorical labels as an estimate of its 597 explanatory power. On the other hand, Astle et al. (2019) used unsupervised 598 self-organization map to classify children into four groups (typically developing, 599 broad cognitive deficits in both language and mathematics, working memory 600 problems, and phonological difficulties). These alternative approaches can shed 601 light on the search for more effective methods for predicting academic 602 achievement.

603 Fifth, a critical step for any neuroimaging studies using machine 604 learning is feature selection. As is clear from our survey of the literature, many 605 studies have relied on the selection of specific regions-of-interest (ROIs) as 606 features to construct machine learning models (see Tables 1-4). A well-known 607 issue with ROI analyses in neuroimaging studies is that the way they are 608 selected might bias the outcome of the analyses. For instance, selecting ROIs 609 based on data that are non-independent from the effect tested might lead to 610 effect sizes that are inflated, an issue known as circular analyses (Kriegeskorte 611 et al., 2009). Several neuroimaging studies (i.e., 15 out of 30 ROI-based

612 studies) reviewed here have selected ROIs based on the same dataset that was 613 used for their machine learning analyses. This may cause inflation of decoding 614 accuracy and result in a lack of generalizability of decoding models, even if 615 ROIs are selected using univariate analyses and subsequently tested with 616 multivariate analyses. The use of non-independent ROIs may further be 617 inconsistent with the assumption of the left-out sample prediction because the 618 test samples are already used for the feature selection during model training. 619 Therefore, studies using non-independent ROIs could be considered as 620 confirmatory, much like those that use in-sample correlations between two 621 datasets (Dumontheil & Klingberg, 2012). Other feature selection methods may 622 be used to circumvent this circularity issue. For example, some have interpreted 623 contributing voxels based on nonzero decoding model weight values (Cui et al., 624 2018; Hoeft et al., 2011) or based on the nested cross-validation (Cui et al., 625 2016). Although caution is needed in interpreting weight values (Haufe et al., 626 2014), both approaches can minimize bias of contributing brain regions. We 627 believe that an interesting approach to avoid circularity issues in feature 628 selection is searchlight decoding analysis (He et al., 2013; Kuhl et al., 2021). 629 This whole-brain analysis constructs decoding model using voxels included in 630 spheres centered around each cortical voxel. This makes it possible to identify 631 brain regions in which multi-voxel patterns are sensitive to the difference 632 between conditions or subject groups (Kriegeskorte et al., 2006).

633 Sixth, because we attempted to provide a comprehensive review of the 634 literature, several studies discussed here rely on relatively small sample sizes 635 (see Tables 1-4). It is now acknowledged that small sample sizes can lead to a 636 significant lack of reliability in neuroimaging data (Button et al., 2013). 637 Therefore, conclusions from these studies must be considered with caution. 638 Indeed, prediction accuracy can largely vary based on sample size. For 639 example, Tamboer et al. (2016) classified dyslexia with 80.0% accuracy in a 640 relatively small group of participants (N = 49) while they obtained 59.0% 641 accuracy in a second group with a much larger sample size (N = 876). In the 642 case of classification between learning disability (dyslexia or dyscalculia) and 643 typically developing participants, no study with a large sample size (N > 100) 644 achieved more than 80% accuracy (Tables S1-2). Usman et al. (2021) did 645 report 94.7% accuracy with N = 148, but this study classified MRI image patches and did not directly classify original brain data. Overall, this suggests 646 647 that a machine learning model with a classification accuracy of 80%, even if the accuracy is significantly higher than the chance level, would lead to
 misdiagnosis in one subject out of five. This is relatively low for real-world
 applications, which should aim for highly accurate predictions more than
 statistical significance.

652 Finally, as is the case generally in neuroimaging research, openly 653 sharing data will be fundamental to improve models predicting academic 654 outcomes from brain data. Building reliable predictive models requires a large 655 amount of data (Varoguaux, 2018). Eight studies constructed predictive models 656 of literacy skills (Table 1) using such open datasets. In addition to the 657 neuroimaging data published in Adolescent Brain Cognitive Development 658 (ABCD) study (Casey et al., 2018) or in UK Biobank (Littlejohns et al., 2020), 659 researchers have published a series of open task-fMRI datasets of school 660 children (Lytle et al., 2019, 2020; Suárez-Pellicioni et al., 2019; J. Wang et al., 661 2022). Such large neuroimaging datasets will be beneficial for future 662 developments in predicting academic performance using machine learning. In 663 addition, acceleration of open data and codes would enable comparison of 664 prediction accuracy across different studies and may reduce inconsistencies 665 between studies.

666

667 Are we getting closer to real-world applicability?

In their review, Gabrieli et al. (2015) highlighted a number of challenges that would have to be met by neuroimaging studies predicting skills to have some real-world applicability, either in the classroom or in a clinical context. These notably included the reliability and representativeness of the findings, the added value compared to behavioral indicators, the economic cost, as well as the ethical and societal issues these methods may raise. We revisit here these challenges nine years after Gabrieli et al. (2015).

675 The section above already fleshes out the critical limitations and 676 challenges in the body of literature. On the one hand, the relative lack of 677 consistency in methodology, experimental designs, and findings shows that 678 there is much room for improvement for studies aiming to translate their findings 679 to the real-world. On the other hand, the literature has significantly expanded 680 over the past ten years. Although initial studies largely focused on literacy skills, 681 investigation of academic skills has now largely expanded to numeracy. In 682 comparison to earlier ones, studies have also now started to focus on longer-683 term outcomes, sometimes over the course of several years (e.g., see Kuhl et

684 al. (2021) for long-term prediction of dyscalculia). This is critical if neuroimaging 685 is to be thought about as a tool for enhancing the detection of future learning 686 difficulties before they occur (Raschle et al., 2012). Finally, recent technical advances in machine learning, as well as the availability of large-scale 687 688 neuroimaging data, might accelerate practical applications. For example, ANNs 689 with a large number of layers were not available 25 years ago (Liu et al., 2022). 690 The development of machine learning toolboxes such as scikit-learn (Abraham 691 et al., 2014) has also reduced the barriers to attempting prediction analyses 692 using neuroimaging data.

693 For neuroimaging measures to be useful indicators for clinical practice 694 or in the classroom, they would of course need to add some explanatory power 695 to the prediction of future academic skills that can already be gathered from 696 behavioral assessments alone. Some studies suggest that a combination of 697 behavioral and brain-based measures may outperform either behavioral or 698 neuroimaging measures alone when predicting academic skills (Beyer et al., 699 2022; Hoeft et al., 2007), though most studies still lack a systematic comparison 700 of prediction based on neuroimaging and behavior.

701 Most studies reviewed here have used MRI to predict academic 702 achievement. Some common criticisms of MRI include its cost and accessibility, 703 as well as the fact that pediatric MRI is relatively challenging. As also pointed 704 out by Gabrieli et al. (2015), it would be important for any financial analysis to 705 account for current practices, which may be costly and less effective as they are 706 often targeted at children who are already failing school. Even though MRI may 707 not be used in the population at large, some studies do suggest that early MRI 708 measures may be useful for some targeted population, for example for children 709 of parents with learning disabilities. Indeed, a large body of evidence indicates 710 that such children are at greater risk of developing the disability than their 711 peers. Brain-based measures, together with behavioral assessments, may thus 712 enhance the early detection of at-risk children (Beyer et al., 2022; Kuhl et al., 713 2021). Another path for reducing the economic cost associated with collecting 714 brain-based measures is a greater reliance on portable and wearable 715 neuroimaging devices, such as wireless EEG or fNIRS. Critically, these 716 methods have been increasingly used over the past ten years, with several 717 studies showing their applicability for collecting brain data in uncontrolled 718 environments such as classrooms (Davidesco et al., 2021). The field is now ripe for testing how these techniques may be combined with machine learning topredict academic outcomes and how they compare to MRI measures.

721 Finally, any use of neuroimaging measures to predict aspects of 722 academic achievement would have to take into consideration ethical and 723 societal issues. Though behavioral measures such as intelligence quotient (IQ) 724 have long been used to predict academic achievement (Chamorro-Premuzic & 725 Furnham, 2008), studies have shown that brain-based measures may have a 726 special status in the public eye and be easily misinterpreted (Racine et al., 727 2005). For example, there is evidence suggesting that people often perceive 728 scientific claims as more credible when they include references to the brain or 729 neuroscientific information (Weisberg et al., 2008), which suggests that people 730 might give more weight to brain-based than behavioral indicators. Another 731 critical aspect of the findings reviewed here is that they may raise ethical 732 questions about whether they could be used to merely identify those with the 733 highest likelihood of success instead of identifying individuals who are at-risk 734 and would need help. Although a discussion of these ethical and societal issues 735 is beyond the scope of the present review, it is clear that they need to be 736 considered by researchers, clinicians, educators, parents, students and policy 737 makers.

738

739 Conclusion

Nine years after the review of Gabrieli et al. (2015), studies using machine 740 741 learning to predict educational achievement and learning disabilities from brain 742 activity have grown exponentially, particularly in the domains of literacy and 743 numeracy. However, we found in this updated review a considerable variation in 744 algorithms and underlying brain circuits between studies. Studies also largely 745 rely on relatively small samples and suboptimal models. We argue that the field 746 needs a standardization of methods, as well as a greater use of accessible and portable neuroimaging methods that have more applicability potential than lab-747 748 based neuroimaging techniques.

749

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765	
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- 1215 **Back matters section** 1216 1217 Data and code availability There are no data or code associated with this article. 1218 1219 1220 Author Contributions: T.N. and J.P. conceptualized the study, T.N., C.T., and 1221 J.P. were involved in the article selection and data extraction, T.N. wrote a 1222 manuscript with critical revisions by J.P. and C.T. 1223 1224 **Acknowledgments** This study was funded by the Agence Nationale de la Recherche (ANR-14-1225 1226 CE30-0002 and ANR-17-CE28-0014), the Fédération pour la Recherche sur le 1227 Cerveau (FRC2022) and the Fondation de France (00123415/WB-2021-38649) to J.P., and by H2020 Marie Skłodowska-Curie Actions (grant number 1228 1229 101023033) and MEXT/JSPS KAKENHI (grant numbers 24H01559 and 1230 24H02172) to T.N. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. 1231 1232 1233 **Competing interests** The authors have declared that no competing interests exist. 1234
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