Development of the Linguistic Evaluation of Prefrontal Synthesis (LEPS) test for children with language delay

Andrey Vyshedskiy, Ph.D., Boston University, ImagiRation LLC, Megan Catherine DuBois, ImagiRation LLC, Emma Mugford, ImagiRation LLC, Irene Piryatinsky, Ph.D., Instructor, Psychiatry, Harvard Medical School,

*Corresponding author: Andrey Vyshedskiy, Ph.D., Boston University, Boston, USA, Tel: +1 (617) 433-7724; E-mail: vysha@bu.edu

Keywords: Differential diagnosis, autism, ASD, psychological evaluations, developmental disorder, language therapy, developmental psychology

Abstract

Prefrontal Synthesis is the conscious, purposeful process of synthesizing novel mental images from objects stored in memory. The ability to perform Prefrontal Synthesis is essential for understanding flexible syntax, spatial prepositions, and verb tenses. In typical children, the timeline of Prefrontal Synthesis acquisition correlates strongly with vocabulary expansion. On the other hand, children with language delay may learn hundreds of words but never acquire Prefrontal Synthesis. In these individuals, tests assessing vocabulary comprehension may fail to demonstrate the profound deficit in Prefrontal Synthesis. We developed a 10-item Linguistic Evaluation of Prefrontal Synthesis (LEPS) test and used it to assess Prefrontal Synthesis in 20 neurotypical children age 2 to 6 years and in three individuals with intellectual disabilities. All neurotypical children age 4 years and older as well as two atypical individuals received the score of 5 or greater out of the maximum possible score of 10. An individual with low-functioning autism received the score of 2. LEPS is copyright-free and takes approximately 10 minutes. As LEPS does not rely on productive language, it may be an especially useful tool for assessment of nonverbal children.

Introduction

Language acquisition is a complex process that involves multiple cortical regions. Linking words with objects is primarily the function of Wernicke's area [1]. Interpreting the grammatical structure of a sentence and assigning word forms to a grammatical group (such as noun, verb, or preposition) is primarily the function of Broca's area [1]. Finally, combining objects from memory according to grammatically imposed rules into a novel mental image is the function of the lateral prefrontal cortex (LPFC) [2,3]. The latter function is commonly called imagination. The term "imagination," however, is ambiguous as it is regularly used to describe any imaginary experience. For example, dreaming is often described as an imaginary experience. Dreaming though is not controlled by the LPFC [4–6]. LPFC is inactive during sleep [4,6] and patients whose

LPFC is damaged do not notice change in their dreams [5]. In order to distinguish the imagination during dreaming from the conscious purposeful LPFC-driven synthesis of novel mental images, we define the latter process as *Prefrontal Synthesis* (we have previously referred to the same process as *Mental Synthesis* [7]). Prefrontal Synthesis is completely dependent on an intact LPFC [8–13] and patients with damage to LPFC often lose their Prefrontal Synthesis function (see below).

By definition, Prefrontal Synthesis is the process executed by the LPFC that involves spatial combination of two or more objects from memory into a novel mental image. Spatial information is primarily encoded in the parietal lobe, whereas object features (color, shape, size, etc.) are primarily encoded in the occipital and temporal lobes. Thus, Prefrontal Synthesis involves LPFC-coordinated changes of neuronal activity in multiple regions of the posterior cortex, sometimes called 'posterior cortex hot zone' [14]. Simpler processes of integration of modifiers and object rotation are also driven by the LPFS, but modify a single object and, therefore, do not fall under the definition of Prefrontal Synthesis. [3]

Prefrontal Synthesis is defined narrowly in order to distinguish it from other components of executive function, such as attention, impulse control, and working memory. Prefrontal Synthesis is not a synonym of problem-solving or fluid intelligence, as complex problems can often be solved via amodal completion [15,16], spontaneous insight [17], integration of modifiers [3] and other mechanisms, that either do not require the LPFC or do not involve combination of objects.

The notion about a special type of imagination different from dreaming and spontaneous insight, which is possibly unique to humans has been entertained by many scientists. This special type of imagination has been described as "ability to invent fiction" [18], "episodic future thinking" [19], "mental scenario building" [20], "mental storytelling" [21], "internal mentation" [22], "mentally playing with ideas" [23], "creative intelligence" [24], "prospective memory" [25], "memory of the future" [26], "counterfactual thinking" [27], "integration of multiple relations between mental representations" [9], "the ability to form nested scenarios" [28], "an inner theatre of the mind that allows us to envision and mentally manipulate many possible situations and anticipate different outcomes" [28], "mental exercises that require tracking and integration of what, in the subject's mind, are temporally separate items of information" [12]. The neurobiologically-explicit definition of this "special type of imagination" avoids ambiguity of descriptive definitions and allows analysis of neurobiological bases of behaviors associated with the presence or absence of Prefrontal Synthesis ability.

Prefrontal Synthesis is highly developed in neurotypical individuals well before the age of six [29], but it is known to be a common challenge for children with Autism Spectrum Disorder (ASD) [2]. As a consequence, ASD symptoms often include a phenomenon called *stimulus overselectivity*, whereby an individual cannot mentally combine disparate objects from memory into a novel image [30–32]. For instance, s/he will have difficulty accomplishing a seemingly trivial task, such as an instruction to "pick up a red crayon that is under the table", which requires to combine three different features, i.e. the object itself (*crayon*), its color (*red*), and its location (*under the table*). The LPFC must then mentally integrate all of these into a new mental image, *a red crayon under the table*, in order to take the correct action. When asked to "*pick up a red crayon under the table*," a child with ASD who is unable to mentally synthesize the crayon with its color and location may attend to the word "crayon" and ignore both its location and the fact that it should also be red, therefore picking up any available crayon. The impaired Prefrontal Synthesis affects virtually every area of an individual's verbal, cognitive and social functioning, including the lack of comprehension of flexible syntax and spatial prepositions [33].

Furthermore, unlike vocabulary acquisition, which can be spread throughout one's lifetime, there is only a short critical period for the development of Prefrontal Synthesis capacity since acquisition of neural networks essential for the LPFC ability to combine new images diminishes greatly after early childhood [2]. As a result, 30-40% of individuals diagnosed with ASD experience lifelong impairment in the ability to understand flexible syntax and spatial prepositions [34]. These individuals, commonly referred to as having low-functioning ASD, typically exhibit full-scale IQ below 70 [35,36] and usually perform below the score of 85 in non-verbal IQ tests [36]. In fact, the ability to perform Prefrontal Synthesis and the capacity of understanding the flexible syntax and spatial prepositions, which is associated with it, may be the most salient differentiator between high-functioning and low-functioning ASD.

The ASD community is very aware of this early critical period, and there is a wide consensus that intense early intervention should be administered to children as soon as they are diagnosed with ASD [37]. The goals of speech language pathologists (SLP) and Applied Behavioral Analysis (ABA) therapists happen to be built around the construct of Prefrontal Synthesis, and therefore it is highly targeted in these treatments. SLPs commonly refer to Prefrontal Synthesis developing techniques as "combining adjectives, location/orientation, color, and size with nouns," "following directions with increasing complexity," and "building the multiple features/clauses in the sentence" [38]. In ABA jargon, these techniques are known as "visual-visual and auditory-visual conditional discrimination" [39–42], "development of multi-cue responsivity" [31], and "reduction of stimulus overselectivity" [32].

Despite the widespread recognition of the importance of early development of Prefrontal Synthesis abilities, there is a lack of awareness of the definition and underlying neurology of Prefrontal Synthesis. There is also a lack of psychometric tests that have the ability to measure a child's progress in acquisition of Prefrontal Synthesis. Most language assessment tests rely heavily on a child's vocabulary: Wechsler Intelligence Scale for Children (WISC-V) [43], Peabody Picture Vocabulary Test (PPVT-4) [44], Expressive Vocabulary Test (EVT-2) [45], Clinical Evaluation of Language Fundamentals (CELF-5) [46], Preschool Language Scales (PLS-5) [47], and are therefore an inadequate gauge to assess the Prefrontal Synthesis acquisition. On the other hand, most non-verbal tests such as nonverbal IQ tests (TONI-4 [48,49], WISC-V [43], Raven's Progressive Matrices [50,51]), rely on paper-printed matrix logic that is not accessible to some individuals. Furthermore, these nonverbal tests are not focused specifically on Prefrontal Synthesis, but include categorization, memory, and attention tasks. Therefore, various research groups have used different tests to study Prefrontal Synthesis-like abilities in children, which makes it difficult to compare their results.

For example, Grimshaw *et al.* (1998) studied a 19-year-old man referred to as E.M. E.M. was born profoundly deaf and grew up in a rural area where he was not exposed to any formal sign language [52]. He and his family used homesign, a system of gestures that allowed them to communicate simple commands, but lacked much of syntax. This is quite typical of families with deaf children and hearing parents who are isolated from a sign language community. Instead of learning a formal sign language, they spontaneously develop a homesign system. At the age of 15, E.M. was fitted with hearing aids that corrected his hearing loss and he began to learn verbal Spanish. When Grimshaw *et al.* tested E.M. at age 19, his performance on simple linguistic tests was reasonably good, but his performance on more complex tests was very poor. E.M. had significant difficulty with spatial prepositions. Grimshaw *et al.* reported that "even at the 34-month assessment, he [E.M.] had not mastered one of these prepositions, nor were his errors limited to related pairs (under vs. over, in front of vs. behind). His general strategy when performing this subtest [following a direction to 'put the green box in the blue box'] was to pick up the two appropriate objects and move them through a variety of spatial arrangements, watching the examiner for clues as to which was correct" [52].

One of the most extensive evaluations of the function that we call Prefrontal Synthesis was conducted by Susan Curtiss in her analysis of language in Genie, a young girl who was linguistically isolated until the age of 12.7 [53]. Curtiss' battery of tests included over 20 verbal tasks intended to measure the extent to which Genie understood different aspects of language, including spatial prepositions, singular and plural sentences, negations with *un*, active vs. passive verb tense, superlatives, comparatives, and *wh-* questions. For example, in a test intended to measure Genie's understanding of singular vs. plural nouns, Curtiss would present Genie with two pictures – one with one balloon and another with multiple balloons – and ask her to point to the picture of the balloon or balloons. Similarly, in a test intended to measure Genie's understanding of superlatives, Curtiss would give Genie a picture of five buttons, each varying in size. Genie would be asked to point to the *smallest* or *largest* button, thereby indicating an understanding of superlative language. All of Curtiss' other tests were structured this same way: Genie would be presented with objects or a picture of objects, given a question with a verbal instruction on which object/image to select, and asked to point or select accordingly. Similarly to E.M., Genie's performance on simple tests was reasonably good, but her performance on more complex tests was very poor. Genie never learned to understand spatial prepositions, flexible syntax, and active vs. passive verb tense, i.e. functions that rely on Prefrontal Synthesis.

Alexander Luria worked extensively with adult patients whose Prefrontal Synthesis ability was compromised following a brain lesion. He reports that "these patients had no difficulty grasping the meaning of complex ideas such as 'causation,' 'development,' or 'cooperation.' They were also able to hold abstract conversations. But difficulties developed when they were presented with complex grammatical constructions which coded logical relations. ... Such patients find it almost impossible to understand phrases and words which denote relative position and cannot carry out a simple instruction like 'draw a triangle above a circle.' This difficulty goes beyond parts of speech that code spatial relations. Phrases like 'Sonya is lighter than Natasha' also prove troublesome for these patients, as do temporal relations like 'spring is before summer'. Additionally, patients with this type of lesion have no difficulty articulating words. They are also able to retain their ability to hear and understand most spoken language. Their ability to use numerical symbols and many different kinds of abstract concepts also remains undamaged. They can repeat and understand sentences that simply communicate events by creating a sequence of verbal images, such as: 'One sunny day it was absolutely quiet in the forest. The fir trees were not stirring. Flowers were sprinkled through the fresh, green grass.' Their particular kind of aphasia becomes apparent only when they have to operate with groups or arrangements of elements. If these patients are asked, 'Point to the pencil with the key drawn on it' or 'Where is my sister's friend?' they do not understand what is being said. As one patient put it, 'I know where there is a sister and a friend, but I don't know who belongs to whom'." [54]

The common thread in these different tests — stacking boxes used by Grimshaw *et al.* with subject E.M. [52], flexible syntax tasks used by Curtiss with Genie [53], and simple mental reasoning used by Luria [54] — is that the solution involves mental simulation. A subject is expected to mentally arrange objects from memory into novel mental images. A subject's inability to come up with correct answers is consistent with a functional deficiency, otherwise characterized as a

Prefrontal Synthesis disability. Thus, a consistent Prefrontal Synthesis test could provide a new window into subjects' mind and reconcile observations between different research groups. Accordingly, the goal of this article was to develop a quick test to assess Prefrontal Synthesis ability, specifically Prefrontal Synthesis ability in children with language delay.

Methods

The Linguistic Evaluation of Prefrontal Synthesis (LEPS) test is rooted in a set of common language comprehension items whereby the participants are required to follow verbal commands of increasing difficulty. The purpose of each item was to determine whether an individual could integrate and imagine several objects together, thereby indicating the level of overall Prefrontal Synthesis abilities. All items were scored as either ***1:*** **participant has demonstrated an understanding of the item,** or ***0*****: participant has not demonstrated an understanding of the item**.

The LEPS total score was calculated based on the number of items completed correctly. A total score of 10 indicated that a participant demonstrated an understanding of all items. Similarly, a participant who demonstrated an understanding of seven items would receive a total score of 7, a participant demonstrated an understanding of no items would receive a total score of 0, and so on.

The entire test was designed to take approximately 10 minutes to complete. A detailed description of each LEPS test item is provided below.

1. Integration of modifier

Integration of modifiers in a single object requires the participants to integrate a noun and an adjective. Participants were asked to select an object (e.g. *long red* straw) placed among several decoy objects including other *red* shapes (Lego pieces, small *red* animals) and *long/short* straws of other colors, thus forcing the participant to notice and integrate color, size and object. Colored straws were obtained from https://www.amazon.com/gp/product/B0721B4BJJ.

Prior to completing this item, participants were asked to point to and name the color of various objects to confirm that they understand the word for specific colors. Participants were then asked to complete four tasks in which colors, sizes, and nouns were varied randomly (Table 1, 'Task examples'). Participants needed to answer correctly at least 3 out of 4 tasks (75% accuracy) to receive a score of *1* for this item. This 75% accuracy threshold was chosen to accommodate possible lapses in attention. With six colors, two sizes and three nouns, the probability of answering 75% of tasks correctly by chance is 0.004%. Thus, participants who made 1 error out of 4 tasks were highly unlikely to use the trial-and-error and, therefore, demonstrated general understanding of the item.

2. Stacking cups

A set of colored cups (https://www.amazon.com/dp/B00GIPIM1U) was used for this test. The purpose of this task was to determine whether participants could properly arrange two cups, based on verbal instructions. Before the test, participants were given a demonstration of how to "put the *blue* cup inside the *red* cup" and, if necessary, were helped to stack the cups correctly. This training session with the *blue* and *red* cups was repeated while randomly switching the cup's order until the participant was able to stack the correct cups on their own with no errors.

Once subjects were comfortable stacking the two training cups, they were asked to stack four cups of various color combinations (Table 1, 'Tasks' column). Once the cups were stacked, each task was recorded as correct or incorrect. After each task, the tester encouraged the child by saying "Good job," but no feedback was given concerning correctness of the answer in order to prevent the child from memorizing the answers.

Participants needed to answer correctly at least 3 out of 4 tasks (75% accuracy) to receive a score of *1* for this item. With four cup colors, the probability of answering 75% of tasks correctly by chance is 0.01%.

3. Flexible syntax with stacking cups

The directions for stacking cups were varied syntactically from the previous item. For example, participants were instructed: "inside the blue cup, put the green cup" or "into the red cup, put the green cup." This was intended to be a more difficult item than a conventional instruction like "put the green cup inside the blue cup." Variation in syntax reduced the possibility that participants automatically remembered the instructions they were previously trained on in their language therapy and used this information to complete the item.

Participants needed to answer correctly at least 3 out of 4 tasks (75% accuracy) to receive a score of *1* for this item. With four cup colors, the probability of answering 75% of tasks correctly by chance is 0.01%.

4. Flexible syntax with plush animals

For this item, a set of puppet-like plush animals (giraffe, lion, elephant, and monkey https://www.amazon.com/gp/product/B075KRKPQ7) were laid on a flat surface. Each participant was asked to name the animals to confirm basic knowledge of animal names. Participants were shown an example of what it would look like if "the lion ate the monkey." This was demonstrated by pushing the monkey inside of the lion. For this item, participants were instructed to manipulate objects to show the experimenter what it would look like if "the elephant ate the lion" or if "the lion ate the elephant" and other similar variations.

Identically to all other items, at least 75% accuracy was required to earn a score of *1*. With four animals, the probability of answering 75% of tasks correctly by chance is 0.01%.

5. Passive verb tense with plush animals

This item used the same plush animals, but sought to measure whether the participant could still correctly position one animal inside of another when the directions were given in passive verb tense. For example, participants were prompted with the directions: "the giraffe was eaten by the lion." This decreased the likelihood that participants could follow a rigid syntax algorithm (the first animal is the predator; the second animal is the prey). Since the positions of the predator and the prey in a sentence vary randomly, participants are more likely to actually imagine which animal ate the other.

Again, at least 75% accuracy was required to earn a score of *1*. With four animals, the probability of answering 75% of tasks correctly by chance is 0.01%.

6. Flexible syntax with spatial prepositions

In this item, participants were instructed to maneuver the plush animals according to the spatial prepositions *on top of* and *under*. Before the test, participants were given a demonstration of how to "put the monkey *on top of* and *under* the lion" and, if necessary, were helped to stack the animals correctly. This training session with the monkey and lion was repeated while randomly switching the order of animals until the participant was able to stack the animals on their own with no errors. Once subjects were comfortable stacking the two training animal, participants were asked to show "the giraffe under the monkey," or "the elephant on top of the giraffe." The monkey and the lion pair was not used in the actual test.

The spatial prepositions *behind* and *in front of* were not used to avoid confusion of whether the perspective was from the experimenter or the participant.

Participants needed to answer correctly at least 3 out of 4 tasks (75% accuracy) to receive a score of 1 for this item. With four animals, the probability of answering 75% of tasks correctly by chance is 0.01%.

7. Recursion with spatial prepositions

Recursion with spatial prepositions was also used to verbally indicate the position of the plush animals. Participants were instructed in the following way: "show me: the monkey is under the lion and on top of the giraffe." The instructions always used the middle animal as the point of reference so that the participant had to mentally integrate both aspects of the direction to arrange the animals.

Identically to all other items, at least 75% accuracy was required to earn a score of *1*. With four animals, the probability of answering 75% of tasks correctly by chance is 0.00007%.

8. Mental size comparison

This item included verbal questions in which participants were asked to tell the tester which animal was bigger than the other. For example, the participants were asked "which animal is bigger: the elephant or the chicken?" or "the cat or the mouse?" or "the cat or the lion?" In this item, participants had to determine which animal was bigger than the other by using their own mental representations of animals, without the use of physical representations.

Again, at least 75% accuracy was required to earn a score of *1*. The probability of answering 75% of tasks correctly by chance is 25%.

9. Mental reasoning - animals

In the final two items, participants were asked to synthesize multiple pieces of information to solve simple mental reasoning tasks. No tangible objects were used as representation. In this item, the task was about animal predation. For example, the prompt could be: "if the monkey ate a snake, who is alive?" or "if a lion was eaten by a snake, who is alive"? Instructions for this item included both passive and active verb tenses, which added an extra level of difficulty. Identically to all other items, at least 75% accuracy was required to earn a score of *1*. The probability of answering 75% of tasks correctly by chance is 25%.

10. Mental reasoning - cups

In the final item, the task required participants to imagine stacking cups. For example, the prompt could be: "imagine the red cup inside the green cup, which cup is at the bottom?" or "imagine the blue cup inside the yellow cup, which cup is on top"? Again, at least 75% accuracy was required to earn a score of *1*. The probability of answering 75% of tasks correctly by chance is 25%.

Table 1. LEPS items and example questions

Item	Tasks
1. Integration of Modifiers	1: Give me a *long red* straw 2: Give me a *short green* straw 3: Give me the *small red* Lego 4: Give me the *long blue* Lego
2. Stacking Cups	1: Put the *green* cup inside the *blue* cup 2: Put the *red* cup inside the *green* cup 3: Put the *green* cup inside the *orange* cup 4: Put the *orange* cup inside the *blue* cup
3. Flexible Syntax with Cups	1: Inside the *blue* cup, put the *green* cup 2: Move the cups so that the *orange* cup is inside the *green* cup 3: Move the cups so that the *orange* cup is inside the *green* cup 4: Imagine the *green* cup inside the *red* cup. Move the cups to show this
4. Flexible Syntax with Plush Animals	1: Show me: the *giraffe* ate the *elephant* 2: Show me: the *lion* ate the *monkey* 3: Show me: the *monkey* ate the *giraffe* 4: Show me: the *elephant* ate the lion
5. Passive Verb Tense with Plush Animals	1: Show me: the *lion* was eaten by the *giraffe* 2: Show me: the *monkey* was eaten by the *elephant* 3: Show me: the *giraffe* ate the *monkey* 4: Show me: the *elephant* was eaten by the *lion*
6. Flexible Syntax with Spatial Prepositions and Plush Animals	1: Put the *giraffe* under the *monkey* 2: Place the *elephant* on top of the *giraffe* 3: Put the *lion* on the *elephant* 4: Place the *monkey* under the *lion*
7. Recursion with Spatial Prepositions and Plush Animals	1: Put the *monkey* under the *lion* and on top of the *giraffe* 2: Place the *lion* on top of the *giraffe* and under the *elephant* 3: Move the *monkey* so that it is under the *lion* and on top of the *elephant* 4: Put the *elephant* on top of the *giraffe* and under the *monkey*
8. Mental Size Comparison	1: Imagine an *elephant* and a *chicken*. Which one is bigger? 2: Imagine a *mouse* and a *cat*. Which one is bigger? 3: Imagine a *lion* and a *cat*. Which one is bigger? 4: Imagine a *chicken* and a *cow*. Which one is bigger?
9. Mental Reasoning – Animals	1: If a *monkey* ate a *lion*, which one is still alive? 2: If a *dog* was eaten by a *cow*, which one is still alive? 3: If a *dog* ate a *cow*, which one is still alive? 4: If a *bear* was eaten by a *mouse*, which one is still alive?

10. Mental Reasoning – Cups	1. Imagine the *red* cup inside the *green* cup, which cup is at the bottom? 2. Imagine the *blue* cup inside the *yellow* cup, which cup is on top? 3. Imagine the *blue* cup inside the *red* cup, which cup is on the bottom? 4. Imagine the *yellow* cup inside the *green* cup, which cup is on top?

Response media: physical objects or pictures

Tangible objects were used for the test in all but one participant. Mike, a 10-year-old nonverbal male with ASD, was not able to demonstrate understanding of *instructions* with tangible objects due to a motor deficit. He, therefore, was asked to respond by pointing to pictures (Figures S1 – S5).

Neurotypical participants

A convenience sample of neurotypical participants were obtained for this study by approaching parents of young children in local parks and asking if they would be willing to let a researcher administer the test to their child. The majority of neurotypical participants were obtained from parks in an affluent suburb of Boston, indicating that the convenience sample represents a relatively privileged population. All participants' caregivers consented to anonymized data analysis and publication of the results, and were present during test administration. The mean age of neurotypical participants was 4.3 (range 1.8-6.9). 67% of neurotypical participants were male.

Atypical participants

LEPS test was also used with three atypical individuals: John, Mike, and Peter (pseudonyms). John and Mike had diagnosis of ASD and Peter had diagnosis of ADHD. Each atypical individual's case study is described below. All raw scores on individual measures administered to children described below were converted to standardized scores using test-specific normative data for the patient's age at testing. Standardized scores have a mean of 100 and a standard deviation of 15 (68% of the norm group has scored between 85 and 115). The reported subdomain scores of the Vineland Adaptive Behavior Scale, Second Edition (Vineland-II) are nor standardized. They have population mean of 15 and a standard deviation of 3.

John - a 17-year-old male with ASD

John is a 17-year-old male with ASD. He is the only child of a doctor and a nurse and has lived most of his life in the greater Boston area. His parents immigrated to the United States from Russia before John was born, and as such his native language is Russian. John's parents grew concerned of extreme hyperactive behavior and deficits in social response and communication around age 2. John received an initial diagnosis of Pervasive Developmental Disorder (PDD) with the potential for a diagnosis with ASD at age 2 years and 7 months. Throughout his childhood, quirks in behavior and social coping developed into significant aggression and inattentive behavior that eventually have put him and others around him at high risk for injury.

John's preschool-age development was characterized by intense hyperactivity, fascination with specific toys and shapes, self-stimulation, and significant delays in social engagement, following instructions, and communication. Numerous aspects of his behavior were behind that of a neurotypical child his age. John struggled to maintain eye-contact and his language was primarily echolalic. In addition to this atypical verbal communication, John demonstrated substantial delays in his receptive communication despite normal auditory and vocal abilities.

By the age of 6 years, John needed high levels of supervision and support to function in the school system. At that time, he received 2+ hours a day of intensive ABA, as well as additional help and accommodations in academic and social activities. He showed signs of emerging communication and social awareness with others, but still spoke in short sentences that did not include descriptive language. His receptive, expressive, and pragmatic language was below that of a normal child his age, but he did show moderate progress in some areas. He had difficulty understanding complex or abstract directions, as well as long sentence structures and vocabulary. He could comprehend some spatial prepositions (e.g. in/out, up/down) but not others (e.g. in front of, next to). Much of John's language was still echolalic, but he could utter appropriate phrases from time to time.

John's language was evaluated multiple times by the Preschool Language Scale - Fourth Edition (PLS-4). PLS-4 is a standardized test with norms available for age of 0 to 8 years. At the age of 4 years, John received an Auditory Comprehension score of 76 (5^{th} percentile), and an Expressive Communication score of 76 (5^{th} percentile), falling to the 3-year 10-month and 3-year 5-month age level, respectively. At the age of 6 years, he received an Auditory Comprehension score of 50 (<0.1 percentile), and an Expressive Communication score of 50 (<0.1 percentile), falling at the 3-year 9-month and 3-year 5-month age level, respectively, indicating a drop in performance over a three-year period.

Also at the age of 6 years, John's functional use of language was evaluated using the parent-reported Vineland Adaptive Behavior Scale, Second Edition (Vineland-II). John's standardized score on the Communication subscale was 72 (3^{rd} percentile). Within the Communication subscale, John received a Receptive Communication subdomain V-scale score of 11 and an Expressive Communication subdomain V-scale score of 9, both falling to the 2-year 10-month age level. On these subdomain V-scale scores a population mean is 15 and a standard deviation is 3 (scores between 13 and 17 reflect an adaptive level that falls within the adequate range). These scores are similar to John's performance on the Vineland-II during the previous year, indicating a lack of progress on adaptive language capabilities.

By the time John was 7 years old, his behavior reflected significant regression in certain aspects of his former progress. At this time, his Communication subscale standardized score fell to 67 (1^{st} percentile), while his Receptive Communication subdomain V-scale score fell to 9, and his Expressive Communication subdomain V-scale score fell to 9. This corresponds to the level of a typical two-year and two-month-old child. His non-compliant, self-stimulating behavior consistently hindered his ability to function. He exhibited little progress in language, adaptability, and social coping, and his inattention made it near impossible to test his cognitive capabilities.

By late childhood, John was under constant supervision and required a very strict schedule (including what he does during his "break" times). He exhibited extremely aggressive behaviors, such as hurling and kicking small and large objects across various rooms and pulling down his pants, as well as some more serious events that placed both John and others' physical and mental health at serious risk. It was decided from observing John's behavior in school and at home that he needed a full-time residential placement in a setting designed for children with autism to prevent further damage.

Currently, John resides in a full-time residential facility and spends weekends at home with his parents. In line with John's Individualized Education Plan (IEP), this program allows for 1:1 attention throughout the day and seeks specific outcomes for growth. Areas of attention include language, mathematics, social behavior, self-help skills, physical health, and recreational activities. In the past, John has received a number of different medications to address his hyperactivity and aggression, such as Risperdal, Baclofen, Adderall, Valproic acid, and Abilify. At the time of his LEPS testing John received 8 mg of Abilify twice a day.

Peter – a 7 year-7 month-old fully verbal male with ADHD

Peter is a male who exhibits significant difficulty following simple and complex instructions and remaining attentive. He was tested at the age of 7 years and 7 months. He lives in the Boston area with his parents and two brothers. Peter's mother grew concerned of his clumsiness and short attention span when he was in preschool, and sought evaluations to determine whether it was caused by forgetfulness or an inability to understand instructions. Peter received a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD combined type – both inattentiveness and hyperactivity) at age 6 years 10 months. Peter was also diagnosed with an Unspecified Communication Disorder and a Developmental Coordination Disorder, reflecting his language and motor delays. Despite this, Peter currently plays well with the other kids of his age and has no difficulty making friends. He is extremely talkative, and does not appear atypical or inhibited in the way he interacts with his environment and those around him (e.g. makes eye contact, enjoys being outside and being active, etc.). Peter's parents describe him as a happy and easy-going boy. However, he fidgets constantly and is easily distracted by outside stimuli. Peter is unable to efficiently complete tasks at school and at home because he becomes easily frustrated when something requires his focus and attention for any extended period of time. Additionally, he exhibits delays in receptive and expressive language development. Most notably, he is unable to understand complex directions and questions, and responds to questions with short, simple sentences.

The Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (WPPSI-IV) was administered to measure Peter's cognitive abilities. He received a standardized IQ score of 79 (8^{th} percentile), which falls within the Borderline range. This indicated a clinically significant deficit in overall intellectual abilities. Within the WPPSI-IV, Peter received a score of 74 (4^{th} percentile) on the Fluid Reasoning Index, which measured nonverbal reasoning skills. The Wechsler Individual Achievement Test, Third Edition (WIAT-III) was used to measure Peter's educational performance. The test results indicated that most of Peter's educational abilities are at the Kindergarten level, slightly below a normal level for his age. The results of this IQ measures, as well as clinical observations of Peter's behavior, was in line with his mother's reports that he struggles with behavioral inhibition, attention, and certain aspects of executive function. On the parent-reported Vineland-III, Peter received a standardized Communication score of 75 (5^{th} percentile)). Peter does not yet meet criteria for an intellectual disability; however, his ADHD severely inhibits his performance at school. At the time of LEPS test, ADHD was diagnosed, but Peter was not taking any medications yet.

Mike – a 10 year-4 month-old nonverbal male with ASD

Mike is a 10-year-old non-verbal male with ASD who communicates via iPad. He lives in the Boston area with his parents and siblings and attends a local public school. He is easily aroused by sensory stimuli and engages in stereotypical self-stimulating behavior, such as squeezing and folding his hands together. These gross motor problems have been present since birth and inhibit his ability to concentrate on tasks and carry out daily functions. Additionally, his self-stimulating behaviors affect many aspects of functioning, such as the ability to sit still and engage in conversation with others. The parent and teacher-completed Behavioral Symptom Index indicated that Mike's atypicality, hyperactivity, attention problems, and withdrawal are all at the Clinically Significant range. Because of this, he has utilized an Individualized Education Program (IEP) since preschool. This includes additional 1:1 therapy in speech-language, occupational therapy, academics, and adaptive PE. Mike's primary challenges are functional communication and extreme deficits in the use of fine and gross motor skills. Recent evaluations showed that he has a well-developed vocabulary and ability to recall words. He is also capable of simple addition and multiplication. Mike is able to correctly respond to standard test items, but it is difficult for him to respond verbally or using complex actions/gestures without accommodations.

A number of formal assessment measures were administered to Mike, most notably the parent/teacher-reported Vineland Adaptive Behavior Scales-Third Edition (Vineland-III). Mike's standardized score for Communication subscale fell at a 62 (1^{st} percentile). Within the Communication subscale, Mike received a Receptive Communication subdomain V-scale score of 12 from his mother and 7 from his teacher, and a Expressive Communication subdomain V-scale score of 9 from his mother and 1 from his teacher (population mean = 15, standard deviation = 3).

Mike received low average/average scores on most measures of cognitive function, but fell at the borderline impaired range with standardized score of 74 (4^{th} percentile) on the Visual-Spatial Processing measure. Within this measure, Mike's performance on various visual-spatial processing subscales ranged from age-appropriate (verbal) to well below average (nonverbal). It is important to note that on the verbal portion of the test, Mike was allowed to respond with a number and letter board instead of responding verbally. If he was required to respond verbally, he would have performed significantly lower. These scores and behavioral observations reflect Mike's visible atypical behaviors and show that he falls below a normal age range in many tasks and cognitive functions.

Results

Twenty neurotypically and three atypically developing individuals were tested with the LEPS test. Each item aimed to determine whether an individual could integrate and imagine several objects together, thereby indicating the level of overall Prefrontal Synthesis abilities. Using variations in sentence structure for each verbal instruction, every subject was asked to complete several tasks in each item. All items were scored as either *1:* participant has demonstrated an understanding, or *0*: participant has not demonstrated an understanding.

Participant (age/gender)	Item Number										
	1.Integra-tion of modifiers	2.Stack-ing cups	3. Flexible Syntax w/cups	4.Flexible syntax w/ animals	5. Passive vs. active w/ animals	6. Flexible syntax w/ spatial prep.	7.Recur-sion w/spatial prep.	8. Mental size comparison	9 Mental reasoning – animals	10. Mental reasoning – cups	Total
1 (2.2/F)	1	1	0	0	0	0	0	0	0	0	2
3 (2.3/F)	0	0	0	0	0	0	0	0	0	0	0
3 (2.3/M)	0	0	0	0	0	0	0	0	0	0	0
4 (2.5/M)	0	0	0	0	0	0	0	0	0	0	0
5 (2.7/M)	0	1	0	0	0	0	0	0	0	0	1
6 (2.7/F)	0	0	0	0	0	0	0	0	0	0	0
7 (2.8/F)	1	0	0	0	0	0	0	0	0	0	1
8 (2.8/M)	1	1	0	0	0	0	0	1	0	0	3
9 (3.8/F)	1	1	1	1	0	0	0	1	0	0	5
10 (3.9/F)	1	1	1	1	1	0	0	1	1	0	7
11 (4.0/F)	1	1	1	1	1	1	0	1	1	0	8
12 (4.2/M)	1	1	1	1	1	1	1	1	1	1	10
13 (4.4/F)	1	1	1	1	1	1	0	1	1	0	8
14 (4.5/M)	1	1	0	1	0	1	1	1	1	1	8
15 (4.5/F)	1	1	1	1	1	1	1	1	1	0	9
16 (4.7/M)	1	1	1	1	1	1	1	1	1	1	10
17 (5.0/F)	1	1	1	1	1	1	1	1	1	1	10
18 (5.3/M)	1	1	1	1	1	1	1	1	1	1	10
19 (5.3/F)	1	1	1	1	1	1	1	1	1	1	10
20 (5.6/F)	1	1	1	1	1	1	1	1	1	1	10
John (17.4/M)	1	1	0	0	0	0	0	0	0	0	2
Peter (7.6/M)	1	1	1	1	0	1	1	1	1	1	9
Mike (10.3/M)	1	1	1	1	1	1	1	1	1	1	10

Table 2. LEPS test performance in neurotypical participants and participants with ASD or intellectual disabilities

1. Integration of modifier

The purpose of this item is to determine whether an individual is able to integrate two different properties of an object (e.g., *give me the long red straw* – find both the long straw and the red straw, thus integrating two properties). All neurotypical children over the age of 2.8 and all three atypical individuals demonstrated an understanding of this item, indicating that each understood the basic properties of an object and could combine nouns and adjectives to select the correct object (Table 2).

John and Peter demonstrated an understanding of this item with tangible objects, but Mike did not. Mike selected objects with correct shape, or color, or size but in none of the 8 trials was he able to select a correct object with the correct color and size. However, Mike was able to point to correct pictures (Figure S1A) with 100% accuracy.

2. Stacking cups test

In this item, participants were tested on their ability to correctly stack two cups in the order instructed. For example, participants were instructed to "put the blue cup inside the green cup."

All neurotypical children over the age of 3 and all three atypical children demonstrated an understanding of this item.

John and Peter demonstrated an understanding of this item with tangible objects, but Mike did not. Mike usually selected the correct cups but stacked them in random order. However, Mike was able to point to correct pictures with 100% accuracy.

3. Flexible syntax with stacking cups

The flexible syntax with stacking cups item was intended to measure whether participants could correctly order two cups when syntax deviated from a conventional structure: e.g. “inside the blue cup, put the red cup.” Neurotypical children over the age of 4.5 were able to do this. It is important to note that in this and other complex items, neurotypical children exhibited a noticeable pause between hearing the instruction and the arrangement of the objects. During this pause, neurotypical children tended to look away from the examiner and the focus of their eyes notably changed.

Peter demonstrated an understanding of this item with tangible objects. John, however, was unable to stack the cups in the correct order or point to a correct picture when the syntax varied. John always selected the appropriate cups, but combined them randomly. John never showed the pause between the instruction and task performance that neurotypical children demonstrated when stacking the cups.

Mike was not able to demonstrate understanding of this item with tangible objects. There was no pause or hesitation in his movements; he simply stacked the cups in random order. However, Mike was able to point to correct pictures with 100% accuracy.

4. Flexible syntax with plush animals

The purpose of this item is to determine whether participants could correctly determine which plush animal ate the other and arrange the animals accordingly based on verbal instructions, such as “the lion ate the monkey.” All neurotypical kids over the age of 3.8 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item with tangible objects. John did not show understanding of this item with either tangible objects or pictures. John always selected the appropriate animals, but combined them randomly. Mike was not able to demonstrate understanding of this item with tangible objects, but pointed to correct pictures with 100% accuracy.

5. Passive verb tense with plush animals

The purpose of this item is to determine whether participants could still order the plush animals when the verb tense changed from active to passive (e.g. “the lion was eaten by the monkey.”) All neurotypical children over the age of 4.5 demonstrated an understanding of this item.

Neither John nor Peter were able to demonstrate understanding of this item with tangible objects or pictures. Mike was not able to demonstrate understanding of this item with tangible objects, but pointed to correct pictures with 100% accuracy.

6. Flexible syntax with spatial prepositions

The purpose of this item is to understand subjects’ ability to follow directions with spatial prepositions, e.g. “show me the monkey under the giraffe.” Neurotypical children over the age of

4.0 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item with tangible objects. John did not show understanding of this item with either tangible objects or pictures. John understood spatial prepositions in the context of a plate and a cup (which was not part of the LEPS test) but failed completely in the context of plush animals. When asked to put the lion *under* or *on top of* the monkey he would take correct plush animals and place them randomly one on top of the other.

Mike was not able to demonstrate understanding of this item with tangible objects, but pointed to correct pictures with 100% accuracy.

7. Recursion with spatial prepositions

Recursion with spatial prepositions is similar to recursion with stacking cups; however, instead of cups, plush animals were used. The purpose is to determine participants' ability to follow prepositional directions to determine where the animals should be located relative to one another, while the directions were always centered on the middle animal. For example, "the monkey is under the lion and on top of the giraffe." All neurotypical children over the age of 4.5 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item with tangible objects, while John did not show understanding of this item with either tangible objects or pictures. Mike was not able to demonstrate understanding of this item with tangible objects, but pointed to correct pictures with 100% accuracy.

8. Mental size comparison

The purpose of this item is to ask the participant to mentally visualize different animals in their mind and determine which one was bigger, e.g. "which animal is bigger, a lion or a cat?" All neurotypical children over the age of 3.0 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item by answering verbally. John was not able to focus on the tasks and answered randomly by calling the names of various animals. Mike responded by spelling the answers on his iPad with 100% accuracy.

9. Mental reasoning – animals

The purpose of this item is to assess whether participants are able to mentally imagine a scene in which one animal ate another, without physical representations of the animals. The instructions used both active and passive verb tenses: e.g., "if the snake ate the lion, who is alive" or "if the snake was eaten by the lion, who is alive." All neurotypical children over the age of 3.9 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item by answering verbally. John was not able to focus on the tasks and answered randomly by calling the names of various animals. Mike responded by spelling the answers on his iPad with 100% accuracy.

10. Mental reasoning – cups

The purpose of this item is to assess whether participants are able to mentally imagine the order of stacked cups without physical representations of them. All neurotypical children over the age of 4.7 demonstrated an understanding of this item.

Peter demonstrated an understanding of this item by answering verbally. John was not able to focus on the tasks and answered randomly by calling the names of various animals. Mike responded by spelling the answers on his iPad with 100% accuracy.

Prefrontal Synthesis acquisition "norms"

Figure 1 summarizes the LEPS total score as a function of age in neurotypical children. Markers indicate individual children LEPS scores. Notice the exponential increase of the LEPS total score between the ages of 3 and 4.

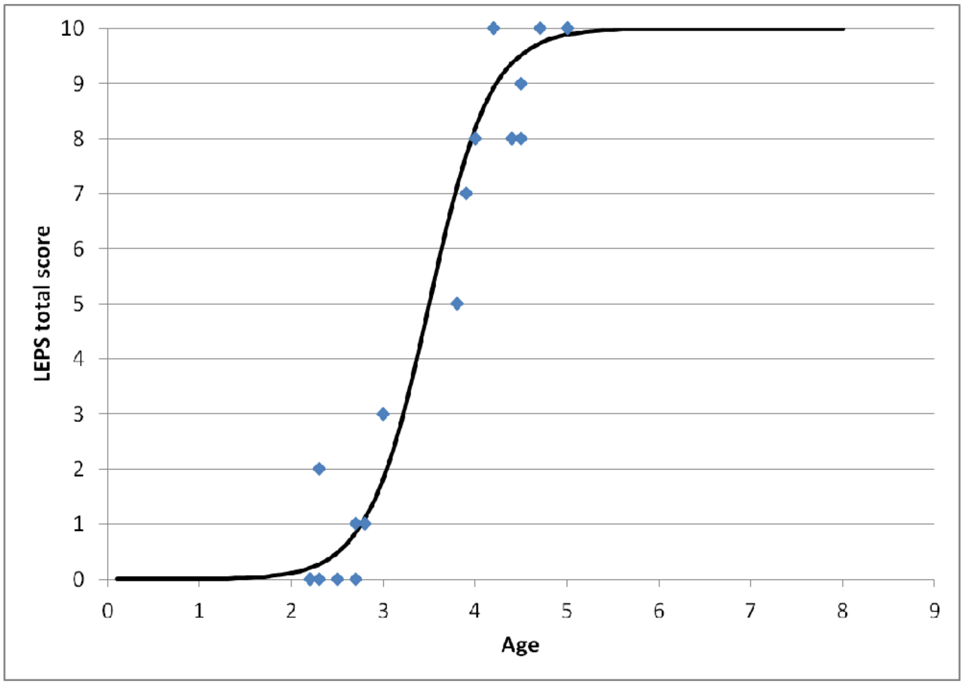

Figure 1. Scatter plot of the LEPS total score as a function of age in neurotypical children. Markers indicate LEPS total scores of individual children.

Discussion

Association of Wernicke's and Broca's areas with language is well-known. Less common is realization that understanding of flexible language depends on the lateral prefrontal cortex (LPFC). Wernicke's area primarily links words with objects [1], Broca's area interprets the grammar and assigns words in a sentence to a grammatical group such as noun, verb, or preposition [1], but only the LPFC can synthesize the objects from memory into a novel mental image according to grammatically imposed rules [2,3]. This latter function may be called *imagination*, but we prefer a more specific term, *Prefrontal Synthesis* in order to distinguish this function from other components of imagination, such as dreaming, simple memory recall, and spontaneous insight. Prefrontal Synthesis is defined as conscious purposeful LPFC-driven synthesis of *novel* mental images from two or more objects stored in memory.

Lesions to the LPFC can result is alteration in language that Fuster calls "prefrontal aphasia" [12] and Luria "frontal dynamic aphasia" [55]. Fuster explains that "although the pronunciation of words and sentences remains intact, language is impoverished and shows an apparent diminution of the capacity to 'propositionize.' The length and complexity of sentences are reduced. There is a dearth of dependent clauses and, more generally, an underutilization of what Chomsky characterizes as the potential for recursiveness of language".

One of the most debilitating features of deficient Prefrontal Synthesis is the inability to understand flexible syntax and spatial prepositions, e.g., to distinguish the sentences such as: "The dog bit my friend" and "My friend bit the dog." Both sentences use identical words and grammar. Understanding the difference in meaning between them and appreciating the humor of the second sentence depends on the LPFC ability to synthesize the two images into a novel mental image. Similarly, understanding of spatial prepositions such as *in, on, under, over, beside, in front of, behind* requires a subject to synthesize several objects into one mental frame. For example, the request "to put a green box {inside/behind/on top of} the blue box" requires an initial mental simulation of the scene, only after which is it possible to correctly arrange the physical objects. An inability to produce a novel mental image of the green box {inside/behind/on top of} the blue box would lead to the use of trial-and-error, which in majority of cases will result in an incorrect arrangement.

In neurotypical children, Wernicke's area develops concurrently with the lateral prefrontal cortex (LPFC), but in the nonverbal children with ASD, development of one cortical area can significantly outpace the other. Commonly, Wernicke's area develops significantly faster than the LPFC and, as a result, the ability to understand words significantly outpaces acquisition of Prefrontal Synthesis and its dependent functions, such as the ability to understand flexible syntax and spatial prepositions [33,36,56,57]. In individuals whose Wernicke's area and LPFC are developing asynchronously, their functions should be measured separately. It is not uncommon to observe the following developmental steps in individuals who acquire language with a significant delay: they start to understand some individual words and phrases, then develop understanding of more complex syntactic language, and only after that they begin to verbally express themselves, first with individual words and then with complete sentences. The existing evaluations adequately assess the former (receptive vocabulary acquisition, Wernicke's area) as well as the latter (expressive language development, Broca's area), but, critically, miss to assess the middle step which heralds the LPFC function of Prefrontal Synthesis and the corresponding understanding of flexible syntax. Therefore, there is a substantial gap in the ability of the existing evaluation tools to faithfully measure a child's developmental progress.

The purpose of this article was to develop and test an evaluation for Prefrontal Synthesis that is suitable for children with ASD and other intellectual disabilities. Prefrontal Synthesis is defined as the purposeful process of synthesizing novel mental images from objects stored in memory and is crucial in understanding flexible syntax, spatial prepositions, and verb tenses [2]. Prefrontal Synthesis assessment in adults has a range of options, such as the Tower of London test [58] and the mental 2-digit number multiplication [59]. However, these tests are not applicable to young children, as they rely heavily on attention and working memory, which tax the PFC beyond abilities of most children, and knowledge of multiplication that is beyond the limits of young children who do not know arithmetic. Accordingly, we developed a 10-item Linguistic Evaluation of Prefrontal Synthesis (LEPS) scale and used it to assess Prefrontal Synthesis in 20 neurotypical children age 2 to 6 and in three atypical individuals. All neurotypical children age 4 years 7 months and older received the maximum possible Prefrontal Synthesis score of 10. In younger children, Prefrontal Synthesis scores decreased with age (Figure 1). Individuals with an intellectual disability received significantly lower Prefrontal Synthesis scores than their neurotypical peers: John, a 17-year-old male with ASD received the score of 2, demonstrating a clear Prefrontal Synthesis disability; Peter, a 7-years 7-months boy with ADHD received the score of 9, indicating nearly full Prefrontal Synthesis abilities; and Mike, a 10-year-old nonverbal male with ASD received the score of 10, indicating normal Prefrontal Synthesis abilities. In the following discussion, we describe our logic for LEPS format and individual items, as well as several notable observations from the development of the measure that provide insight into how and why LEPS can be used to test Prefrontal Synthesis in atypically developing children.

Organization of the LEPS test

Integration of modifiers is the first item of the LEPS test. Neurologically, both integration of modifiers and Prefrontal Synthesis functions are controlled by the LPFC, however, integration of modifiers only involves modification of neurons encoding a single object and, consequently, is simpler than the process of Prefrontal Synthesis of *several* independent objects [60]. In other words, integration of modifiers is not Prefrontal Synthesis, but a developmental precursor to Prefrontal Synthesis. This item was included in LEPS for several reasons. First, it is useful for quick assessment of participant's understanding of colors and sizes - essential elements used throughout the LEPS test. Second, in participants with a Prefrontal Synthesis disability, it is useful to know if at least the precursor to Prefrontal Synthesis has been acquired. Third, the easy task of integration of modifiers is a convenient way to focus the participant on more difficult items. Finally, the integration of modifiers item can be used repeatedly throughout LEPS test to gage participant's attention.

The purpose of the remaining items was to create a series of mental puzzles that varied syntactically from the rigid verbal instructions that could be learned through long-term training. For example, consider item 2 that instructed participants to "put the green cup inside the blue cup." There are two ways to successfully complete this stacking cup instruction. One way to find the solution is to mentally synthesize a novel image of the green cup inside the blue cup, and then, after completing the mental simulation, arrange the physical objects to match the image in the mind's eye. An alternative solution could be obtained algorithmically by following these steps: (1) lift the cup mentioned first; (2) insert it into the cup mentioned second. This type of algorithmic solution does not require Prefrontal Synthesis and therefore is much simpler to perform. It is a sort of automatic routinized action primarily encoded by basal ganglia, akin to riding a bicycle, tying shoelaces, skiing, skating, stopping at a red light, writing a signature, opening a familiar door, or shouting a common expletive.

An example of algorithmic completion of the stacking cup item is provided by John, a verbal 17-year-old individual with ASD. John successfully completed all of the stacking cups questions without making a single mistake. However, John failed all other LEPS items that were no more difficult in grammar, attention, or working memory, thus indicating a Prefrontal Synthesis disability. For example, when instructed "into the {*blue/red/green/yellow*} cup, put the {*green/blue/yellow/red*} cup," John selected the correct cups, but assembled them randomly. Similarly, when asked to demonstrate "the {*lion/elephant/giraffe/monkey*} ate the {*monkey/lion/giraffe/elephant*}," John would select the correct animals, but arrange them randomly. John's performance is consistent with normal attention, but inability to mentally simulate the arrangement of objects according to instructions (Prefrontal Synthesis disability).

How could John stack the cups in item 2 flawlessly without first arranging the cups in his mind's eye? We argue that during 15 years of intensive language therapy, John's stacking cups routine has been automated through frequent training. Consistent with this hypothesis, John completed each stacking movement fast, with no hesitation. Other children normally paused to think while completing the same task, presumably to simulate the answer mentally. The stacking cups/boxes test that could demonstrate a Prefrontal Synthesis deficit in other people, such as E.M. as studied by Grimshaw *et al.* [52], failed to demonstrate the same deficit in John. This is presumably because John was trained extensively during speech and language therapy and could therefore interpret the rigid syntax of item 2 algorithmically.

Naturally, in a test for the LPFC-driven Prefrontal Synthesis, we wanted to avoid giving participants an opportunity to answer items using basal ganglia-driven algorithms as much as possible. If we knew which tasks individuals were trained on, we could have avoided those tasks in the test items. However, it is not feasible for a formal test to avoid all tasks a participant could have been trained on. An alternative to this predicament would be to increase the complexity of the test items. The more complex the items are, the higher is the probability that participants would not have been trained on that particular sentence structure and, therefore, do not have a basal ganglia-based solution algorithm. On the other hand, in developing the test, we wanted to avoid complex grammar that may be unfamiliar to younger participants and to those who are nonverbal or have intellectual disabilities. We also wanted to avoid tasks involving synthesis of many disparate objects that could overwhelm the attention and working memory systems. Accordingly, we tried to use simple grammatical structures and limit the number of independent objects that had to be arranged into a novel position as much as possible.

With these limitations, there is no perfect single test item to unequivocally assess Prefrontal Synthesis. At least theoretically, interpretation of any syntactically rigid sentence structure can be broken into an algorithm, which can be ingrained into an individual's implicit memory. If a participant has been trained on a particular item for an extended period of time, any item in the LEPS test can be performed correctly without imagining a novel combination of objects. Thus, instead of relying on any single item, the LEPS test has 10 items that assess Prefrontal Synthesis, using both flexible syntax and recursion in the hope that most items have not been engrained into participants' basal ganglia. Accordingly, the results of the LEPS test have to be interpreted with all the items considered integrally: the combined score of all items is used to assess participant's Prefrontal Synthesis ability. The higher the LEPS score, the greater the evidence of developed Prefrontal Synthesis ability; correct answers in several items on LEPS test shall not be definitively interpreted as an indicator of Prefrontal Synthesis, especially in individuals with many years of language therapy who could have ingrained interpretation of rigid syntax into context-dependent algorithm.

Physical toys were better than pictures for Prefrontal Synthesis assessment in the ADHD participant

For a typical adult, following an instruction on paper, such as having them to show "a whale ate a man" by pointing to a correct picture, is no harder than arranging physical toys (a whale and a man) in the correct position. This is not the case for some atypical individuals. Consider Peter, a 7 year-7 month-old fully verbal child with ADHD. Peter's performance on paper-based tests was strikingly different from his performance with physical toys. Peter received a standardized score of 74 (i.e. lower than 96% of population) on the Fluid Reasoning Index of the WPPSI-IV, an IQ test in which the participant has to select a picture that represents the correct answer. This score indicates that Peter has failed all questions that test Prefrontal Synthesis. We confirmed these observations by testing Peter with our proprietary paper-based test. Peter showed understanding of the concept of matrix analogies by succeeding in all simple items that required “finding the same objects” and “integration of color, size and number modifiers.” But upon being asked to imagine "the man ate the whale" or “the whale ate the man" and then point to a picture depicting this, Peter answered randomly. Did Peter understand the difference between "the man ate the whale" versus “the whale ate the man?” Although Peter’s performance on the paper-based test was below the chance level, his performance increased to 100% accuracy when he was allowed to show his answer with physical objects (item 5). In fact, Peter has succeeded in all but one LEPS item (he was uncertain of the difference between the passive and active forms of the verb “eat”) and received a LEPS total score of 9. The LEPS test was a superior measurement for Prefrontal Synthesis than the paper-based WPPSI-IV test.

Why Peter was able to demonstrate the understanding of the difference between “the lion ate the monkey” and the “monkey ate the lion” with physical objects in the LEPS test item 5, but failed the equivalent of the same question in a paper-based test: “the man ate the whale” and “the whale ate the man?” Clearly, Peter’s Wernicke’s area was capable of comprehending the meaning of words, his Broca’s area was capable of assigning word forms to a grammatical group (such as noun or verb), and his LPFC was capable of purposeful synthesis of disparate objects (in this case the man and the whale) together. From this, we can speculate that Peter’s ADHD is to blame for his failure in paper-based tasks, since tangible objects have been shown to have a greater influence on attention than objects shown in pictures[61]. It is likely that use of physical toys captured Peter’s attention on the task much more than paper could. Peter was re-tested with our proprietary paper-based test 4 months after the initial test. At that time he was taking 30mg of Ritalin daily. This time Peter answered all paper-based items correctly, including items testing Prefrontal Synthesis.

Peter’s case is also a good demonstration of the dissociation between attention and Prefrontal Synthesis. Both attention and Prefrontal Synthesis are functions of the LPFC. In neurotypical children, attention and Prefrontal Synthesis are acquired concurrently. However, the dissociation of attention and Prefrontal Synthesis may be observed in some atypical individuals. In Peter, Prefrontal Synthesis was normally or nearly normally developed, while there was severe deficit in his attention. On the other hand, in most late first language learners, attention was normally developed [62] while Prefrontal Synthesis was not [2].

In addition, Peter’s performance reflects dissociation between understanding of grammar and Prefrontal Synthesis. As discussed above, assigning heard word forms to a grammatical group and interpreting a form of the verb is primarily the function of Broca’s area [1] while a purposeful imagining of a novel image is driven by the LPFC. Peter has correctly answered nine questions out of ten including recursive questions that required Prefrontal Synthesis of three objects. The only item that Peter answered incorrectly was the one testing understanding of the passive form of the verb ‘to eat’ (e.g. “the lion was eaten by the monkey”). It is hard to explain Peter’s failure by a Prefrontal Synthesis deficit, since Peter answered correctly all other Prefrontal Synthesis questions including question with recursion that required Prefrontal Synthesis of three objects. A more likely explanation of Peter’s failure in this item is the inability of his Broca's area to disentangle the grammatical structure of verb passive form.

LEPS use in children with motor deficits

Mike, a 10 year-4 month-old nonverbal child with ASD, failed to demonstrate understanding of even simplest instructions (such as "give me *long red* straw") by using tangible objects. However, it was clear that Mike has typical-adult-like Prefrontal Synthesis since he was able to answer all items with 100% accuracy when allowed to point to pictures in items 1 to 7 or spell out the answer in items 8 to 10. He also has age-appropriate arithmetic skills, such as simple mental addition, subtraction, and multiplication. He can even do two-digit number addition in his mind. Clearly, Mike's Wernicke's area is capable of comprehending the meaning of words, his Broca's area is capable of assigning word forms to a grammatical group (such as noun or verb), and his LPFC is capable of purposeful synthesis of disparate objects together. Why couldn't Mike demonstrate his understanding of instructions with tangible objects? The answer probably has to do with the motor regions of the cortex.

Mike is very challenged with anything that has to do with purposeful movement - he has had gross motor delays since birth and this is still a major disability. Mike required intensive training of specific gross motor skills that come naturally to typically developing children. His fine motor skills are also still extremely underdeveloped. Mike's mother reported that, "he could never play with toys because it was just so hard for him – not because he didn't want to."

LEPS test was not the first time when Mike was asked to demonstrate his understanding of instructions by manipulating tangible objects. Language therapists in the past have often tried these exercises. Since manipulation of tangible objects is so difficult for Mike, he has probably learned to withdraw in reaction to motor tasks and responds quickly and thoughtlessly in order to reduce the duration of procrastination.

We'd like to note that despite his motor problems, Mike was able to spell out words on his iPad in response to items 8, 9 and 10. The typing movements were somewhat slower than in typical adults, but nearly as smooth and deliberate. Typing did not seem to be difficult or exhaustive for Mike. It is likely that his familiarity with typing made this task much easier compared to the specialized fine and gross voluntary movements required for rearranging tangible objects.

We conclude that it is important to allow children to respond in the media they are comfortable with. Children with ADHD may not be able to respond on paper while perfectly capable of responding with tangible objects, while children with motor deficits may not be able to respond with tangible objects but are fully capable of responding by pointing to pictures and typing. LEPS test can accommodate both groups of children.

LEPS can be used to diagnose Prefrontal Synthesis disability and to monitor Prefrontal Synthesis acquisition in vulnerable children

The importance of early introduction of language to children, both atypical and neurotypical, is widely recognized [63–65]. Vulnerable individuals include children with congenital deafness, ASD, PDD, and any other children with potential for language delay. In the USA, there are laws that aim to identify vulnerable individuals. In 1999, the U.S. Congress passed the "Newborn and Infant Hearing Screening and Intervention Act," which gives grants to help states create hearing screening programs for newborns. Otoacoustic Emissions Testing is usually done at birth, followed by an Auditory Brainstem Response if the Otoacoustic Emissions test results indicated possible hearing loss. Such screening allows parents to expose deaf children to a formal sign language as early as possible and therefore to avoid any delay in introduction to full recursive language. When congenitally deaf children are exposed to full recursive language early, their function of Prefrontal Synthesis develops normally [66].

American Academy of Pediatrics (AAP) recommends universal screening of 18- and 24-month-old children for ASD, and also that individuals diagnosed with ASD begin to receive no less than 25 hours per week of treatment within 60 days of identification [67]. Despite the AAP recommendation, two-thirds of US children on the autism spectrum under the age of 8 fail to get even the minimum recommended treatment [68] because of major problems with the availability, quality, and general funding for early intervention programs [69–71]. Since the AAP's 2007 recommendation of universal early screening, there has been a sharp increase in demand for ASD-related services (58% on average, Ref. [72]. However, according to a recent study, most states have reported an enormous shortage of ASD-trained personnel, including behavioral therapists (89%), speech-language pathologists (82%), and occupational therapists (79%) [72]. In many states children are getting less than 5 hours per week of service [72]. This immense shortage disproportionately affects African American and Latino children [72]. Families of newly diagnosed children often face lengthy waitlists for therapy, leaving children without treatment during the most critical early period of development. Thirty to forty percent of individuals diagnosed with ASD receive inadequate therapy. This can cause lifelong Prefrontal Synthesis disabilities, including impairment in the ability to understand flexible syntax and spatial prepositions. John, one of our three atypical participants, is a prime example of this phenomenon. [20]

Propensity to acquire Prefrontal Synthesis seems to start before the age of two [73], reduces notably after five years of age [74–78], and ceases completely after puberty [2]. As the result of a relatively short critical period, the ability of children to acquire Prefrontal Synthesis can be significantly diminished by the time they enter the public school system. Timely identification of Prefrontal Synthesis acquisition delay could facilitate a more comprehensive understanding of a child's cognitive strengths and weaknesses, which would in turn lead to a more targeted intervention therapy.

Limitations

There is no single perfect measurement technique for Prefrontal Synthesis in children. Simpler tests that rely on common sentence structure ("put the green cup inside the blue cup") can all be trained into automatic algorithms that do not involve creating any novel mental images. More difficult tests, such as the Tower of London [58], require significant attention and working memory that is often acquired at an older age. Still other tests, such as 2-digit number multiplication [59] are not appropriate since children do not know numbers or the concept of multiplication. The LEPS test attempts to strike a balance between common and complex questions to present children with a task of imagining novel combinations of objects in their mind. Certainly, such approach has its limitations.

First, the LEPS test is not applicable to the most children younger than 2.5 years, as those children are not yet familiar with words for colors, sizes, and spatial prepositions *inside*, *on top of*, and *under*. However, older children, even if they were not familiar with some words, can often grasp the meaning of those few words during the test: each object used in LEPS is named and each spatial preposition is explained in a demonstration.

Second, performance in the LEPS test depends on a child's attention and motivation. In this regard the LEPS test is no different from other intelligence tests in which children have to stay focused throughout the test. As discussed above, LEPS' use of physical objects instead of pictures makes it easier for children with attention deficit disorder and can result in a better measure of their fluid intelligence.

Conclusions

We describe a 10-item Linguistic Evaluation of Prefrontal Synthesis (LEPS) test designed for quick assessment of Prefrontal Synthesis function of the prefrontal cortex in children. LEPS items use flexible syntax and language recursive elements such as spatial prepositions to present participants with a set of novel questions that most participants have never encountered before and, therefore, could not remember. The sum of 10 items results in the LEPS total score that ranges from 0 (no Prefrontal Synthesis ability was demonstrated) to 10 (full Prefrontal Synthesis ability). The LEPS total score generated by the LEPS test is an absolute measure, independent of age. LEPS test is copyright-free and usually takes less than 10 minutes. As LEPS does not rely on productive language, it may be an especially useful tool for assessing the development of nonverbal children.

Acknowledgments

We wish to thank Dr. Julia Braverman, Dr. Max Lianski, and Dr. Leo Fridman for productive discussion. We thank Dr. Petr Ilyinskii for scrupulous editing of this manuscript and Benjamin Vyshedskiy for help with testing children and data analysis.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Friederici, A. D. The brain basis of language processing: from structure to function. *Physiol. Rev.* **91,** 1357–1392 (2011).

2. Vyshedskiy, Mahapatra, S. & Dunn, R. Linguistically deprived children: meta-analysis of published research underlines the importance of early syntactic language use for normal brain development. *Res. Ideas Outcomes* (2017). doi:10.3897/rio.3.e20696

3. Vyshedskiy, Dunn, R. & Piryatinsky, I. Neurobiological mechanisms for nonverbal IQ tests:

implications for instruction of nonverbal children with autism. *Res. Ideas Outcomes* **3,** e13239 (2017).

4. Braun, A. R. *et al.* Regional cerebral blood flow throughout the sleep-wake cycle. *Brain* **120,** 1173–1197 (1997).
5. Solms, M. *The neuropsychology of dreams: A clinico-anatomical study*. (L. Erlbaum, 1997).
6. Siclari, F. *et al.* The neural correlates of dreaming. *Nat. Neurosci.* **20,** 872 (2017).
7. Vyshedskiy & Dunn, R. Mental synthesis involves the synchronization of independent neuronal ensembles. *Res. Ideas Outcomes* **1,** e7642 (2015).
8. Christoff, K. & Gabrieli, J. D. The frontopolar cortex and human cognition: evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology* **28,** 168–186 (2000).
9. Waltz, J. A. *et al.* A system for relational reasoning in human prefrontal cortex. *Psychol. Sci.* **10,** 119–125 (1999).
10. Duncan, J., Burgess, P. & Emslie, H. Fluid intelligence after frontal lobe lesions. *Neuropsychologia* **33,** 261–268 (1995).
11. Luria, A. R. *Higher cortical functions in man*. (Springer Science & Business Media, 2012).
12. Fuster, J. *The Prefrontal Cortex, Fourth Edition*. (Academic Press, 2008).
13. Baker, S. C. *et al.* Neural systems engaged by planning: a PET study of the Tower of London task. *Neuropsychologia* **34,** 515–526 (1996).
14. Koch, C., Massimini, M., Boly, M. & Tononi, G. Neural correlates of consciousness: progress and problems. *Nat. Rev. Neurosci.* **17,** 307 (2016).

15. Gerbino, W. & Salmaso, D. The effect of amodal completion on visual matching. *Acta Psychol. (Amst.)* **65,** 25–46 (1987).

16. Weigelt, S., Singer, W. & Muckli, L. Separate cortical stages in amodal completion revealed by functional magnetic resonance adaptation. *BMC Neurosci.* **8,** 70 (2007).

17. Salvi, C., Bricolo, E., Kounios, J., Bowden, E. & Beeman, M. Insight solutions are correct more often than analytic solutions. *Think. Reason.* **22,** 443–460 (2016).

18. Harari, Y. N. *Sapiens: A brief history of humankind*. (Random House, 2014).

19. Atance, C. M. & O'Neill, D. K. Episodic future thinking. *Trends Cogn. Sci.* **5,** 533–539 (2001).

20. Suddendorf, T. & Redshaw, J. The development of mental scenario building and episodic foresight. *Ann. N. Y. Acad. Sci.* **1296,** 135–153 (2013).

21. Irwin, S. O. Embodied being: Examining tool use in digital storytelling. *Tamara J. Crit. Organ. Inq.* **12,** (2014).

22. Andrews-Hanna, J. R. The brain's default network and its adaptive role in internal mentation. *The Neuroscientist* **18,** 251–270 (2012).

23. Diamond, A. & Lee, K. Interventions shown to aid executive function development in children 4 to 12 years old. *Science* **333,** 959–964 (2011).

24. Fuster, J. M. *Cortex and mind: Unifying cognition.* (Oxford university press, 2003).

25. Dobbs, A. R. & Rule, B. G. Prospective memory and self-reports of memory abilities in older adults. *Can. J. Psychol. Can. Psychol.* **41,** 209 (1987).

26. Ingvar, D. H. ' Memory of the future': an essay on the temporal organization of conscious

awareness. *Hum. Neurobiol.* **4,** 127–136 (1985).

27. Roese, N. J. Counterfactual thinking. *Psychol. Bull.* **121,** 133 (1997).

28. Suddendorf, T. TWO KEY FEATURES CREATED THE HUMAN MIND INSIDE OUR HEADS. *Sci. Am.* **319,** 43–47 (2018).

29. Halford, G. S. Can young children integrate premises in transitivity and serial order tasks? *Cognit. Psychol.* **16,** 65–93 (1984).

30. Schreibman, L. Diagnostic features of autism. *J. Child Neurol.* **3,** S57–S64 (1988).

31. Lovaas, O. I., Koegel, R. L. & Schreibman, L. Stimulus overselectivity in autism: A review of research. *Psychol. Bull.* **86,** 1236–1254 (1979).

32. Ploog, B. O. Stimulus overselectivity four decades later: A review of the literature and its implications for current research in autism spectrum disorder. *J. Autism Dev. Disord.* **40,** 1332–1349 (2010).

33. Lovaas, O. I., Schreibman, L., Koegel, R. & Rehm, R. Selective responding by autistic children to multiple sensory input. *J. Abnorm. Psychol.* **77,** 211 (1971).

34. Fombonne, E. Epidemiological surveys of autism and other pervasive developmental disorders: an update. *J. Autism Dev. Disord.* **33,** 365–382 (2003).

35. Beglinger, L. J. & Smith, T. H. A review of subtyping in autism and proposed dimensional classification model. *J. Autism Dev. Disord.* **31,** 411–422 (2001).

36. Boucher, J., Mayes, A. & Bigham, S. Memory, language and intellectual ability in low-functioning autism. *J Boucher DM Bowler Eds Mem. Autism Camb. CUP* (2008).

37. Dawson, G. *et al.* Randomized, controlled trial of an intervention for toddlers with autism:

the Early Start Denver Model. *Pediatrics* **125,** e17–e23 (2010).

38. American Speech-Language-HearingAssociation. Scope of practice in speech-language pathology. (2016).

39. Axe, J. B. Conditional discrimination in the intraverbal relation: A review and recommendations for future research. *Anal. Verbal Behav.* **24,** 159–174 (2008).

40. Michael, J., Palmer, D. C. & Sundberg, M. L. The multiple control of verbal behavior. *Anal. Verbal Behav.* **27,** 3–22 (2011).

41. Eikeseth, S. & Smith, D. P. An analysis of verbal stimulus control in intraverbal behavior: implications for practice and applied research. *Anal. Verbal Behav.* **29,** 125–135 (2013).

42. Lowenkron, B. Joint control and the selection of stimuli from their description. *Anal. Verbal Behav.* **22,** 129–151 (2006).

43. Wechsler, D. Wechsler intelligence scale for children. (1949).

44. Dunn, L. M. & Dunn, D. M. *PPVT-4: Peabody picture vocabulary test*. (Pearson Assessments, 2007).

45. Williams, K. T. Expressive vocabulary test second edition (EVT™ 2). *J Am Acad Child Adolesc Psychiatry* **42,** 864–872 (1997).

46. Wiig, E. H., Secord, W. A. & Semel, E. *Clinical evaluation of language fundamentals: CELF-5*. (Pearson, 2013).

47. Zimmerman, I. L., Steiner, V. G. & Pond, R. E. PLS-5: Preschool language scale-5 [measurement instrument]. *San Antonio TX Psychol. Corp.* (2011).

48. Brown, L., Sherbenou, R. J. & Johnsen, S. K. *Test of Nonverbal Intelligence: TONI.* (Pro-ed

Austin, TX, 1982).

49. Brown, L., Sherbenou, R. J. & Johnsen, S. K. *TONI-3, test of nonverbal intelligence: A language-free measure of cognitive ability*. (Pro-Ed, 1997).

50. Raven, J. C. Mental tests used in genetic studies: The performance of related individuals on tests mainly educative and mainly reproductive. *Unpubl. Master's Thesis Univ. Lond.* (1936).

51. Raven, J. *Manual for Raven's progressive matrices and vocabulary scales Section 3: Standard progressive matrices: introducing the parallel and plus versions of the tests*. (Oxford Psychologists, 1998).

52. Grimshaw, G. M., Adelstein, A., Bryden, M. P. & MacKinnon, G. E. First-language acquisition in adolescence: Evidence for a critical period for verbal language development. *Brain Lang.* **63,** 237–255 (1998).

53. Fromkin, V., Krashen, S., Curtiss, S., Rigler, D. & Rigler, M. The development of language in genie: a case of language acquisition beyond the "critical period". *Brain Lang.* **1,** 81–107 (1974).

54. Cole, M., Levitin, K. & Luria, A. R. *The autobiography of Alexander Luria: A dialogue with the making of mind*. (Psychology Press, 2014).

55. Luria, A. R. Traumatic aphasia. Mouton. *The Hague* (1970).

56. Maljaars, J., Noens, I., Scholte, E. & van Berckelaer-Onnes, I. Language in low-functioning children with autistic disorder: Differences between receptive and expressive skills and concurrent predictors of language. *J. Autism Dev. Disord.* **42,** 2181–2191 (2012).

57. Hudry, K. *et al.* Preschoolers with autism show greater impairment in receptive compared

with expressive language abilities. *Int. J. Lang. Commun. Disord.* **45,** 681–690 (2010).

58. Shallice, T. Specific impairments of planning. *Phil Trans R Soc Lond B* **298,** 199–209 (1982).

59. Zago, L. *et al.* Neural correlates of simple and complex mental calculation. *Neuroimage* **13,** 314–327 (2001).

60. Gabay, S., Kalanthroff, E., Henik, A. & Gronau, N. Conceptual size representation in ventral visual cortex. *Neuropsychologia* **81,** 198–206 (2016).

61. Gomez, M. A., Skiba, R. M. & Snow, J. C. Graspable objects grab attention more than images do. *Psychol. Sci.* **29,** 206–218 (2018).

62. Curtiss, S. Dissociations between language and cognition: Cases and implications. *J. Autism Dev. Disord.* **11,** 15–30 (1981).

63. Eldevik, S. *et al.* Using participant data to extend the evidence base for intensive behavioral intervention for children with autism. *Am. J. Intellect. Dev. Disabil.* **115,** 381–405 (2010).

64. Peters-Scheffer, N., Didden, R., Korzilius, H. & Sturmey, P. A meta-analytic study on the effectiveness of comprehensive ABA-based early intervention programs for children with autism spectrum disorders. *Res. Autism Spectr. Disord.* **5,** 60–69 (2011).

65. Virués-Ortega, J. Applied behavior analytic intervention for autism in early childhood: Meta-analysis, meta-regression and dose–response meta-analysis of multiple outcomes. *Clin. Psychol. Rev.* **30,** 387–399 (2010).

66. Mayberry, R. I. Cognitive development in deaf children: The interface of language and perception in neuropsychology. *Handb. Neuropsychol.* **8,** 71–107 (2002).

67. Maglione, M. A. *et al.* Nonmedical interventions for children with ASD: Recommended guidelines and further research needs. *Pediatrics* **130,** S169–S178 (2012).

68. Hume, K., Bellini, S. & Pratt, C. The usage and perceived outcomes of early intervention and early childhood programs for young children with autism spectrum disorder. *Top. Early Child. Spec. Educ.* **25,** 195–207 (2005).

69. Johnson, E. & Hastings, R. P. Facilitating factors and barriers to the implementation of intensive home-based behavioural intervention for young children with autism. *Child Care Health Dev.* **28,** 123–129 (2002).

70. Bibby, P., Eikeseth, S., Martin, N. T., Mudford, O. C. & Reeves, D. Progress and outcomes for children with autism receiving parent-managed intensive interventions. *Res. Dev. Disabil.* **23,** 81–104 (2002).

71. Jacobson, J. W. Early intensive behavioral intervention: Emergence of a consumer-driven service model. *Behav. Anal.* **23,** 149 (2000).

72. Wise, M. D., Little, A. A., Holliman, J. B., Wise, P. H. & Wang, C. J. Can state early intervention programs meet the increased demand of children suspected of having autism spectrum disorders? *J. Dev. Behav. Pediatr.* **31,** 469–476 (2010).

73. Bick, J. *et al.* Effect of early institutionalization and foster care on long-term white matter development: a randomized clinical trial. *JAMA Pediatr.* **169,** 211–219 (2015).

74. Boatman, D. *et al.* Language recovery after left hemispherectomy in children with late-onset seizures. *Ann. Neurol.* **46,** 579–586 (1999).

75. Basser, L. S. Hemiplegia of early onset and the faculty of speech with special reference to the effects of hemispherectomy. *Brain* **85,** 427–460 (1962).

76. Lenneberg, E. H. The biological foundations of language. *Hosp. Pract.* **2,** 59–67 (1967).

77. Krashen, S. & Harshman, R. Lateralization and the critical period. *J. Acoust. Soc. Am.* **52,** 174–174 (1972).

78. Pulsifer, M. B. *et al.* The cognitive outcome of hemispherectomy in 71 children. *Epilepsia* **45,** 243–254 (2004).