Journal of Neurolinguistics 62 (2022) 101042

Contents lists available at ScienceDirect

Journal of Neurolinguistics

journal homepage: www.elsevier.com/locate/jneuroling

The long-lasting effects of thiamine deficiency in infancy on language: A study of a minimal-pair of twins

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A R T I C L E I N F O

Keywords:
Thiamine deficiency
Language impairment
Syntactic movement
Lexical retrieval
Reading

A B S T R A C T

Thiamine, vitamin B1, is a crucial component in brain development. This study examined the role thiamine plays in the development of language, by examining the long-term effects of thiamine deficiency in infancy. The participants were a young adult who had consumed a thiamine-deficient baby formula at age 1;0–1;5, and her non-identical twin sister, who had consumed a non-deficient formula. We conducted a comprehensive assessment of various language abilities, including syntax, morphology, lexical encoding and retrieval, word and nonword reading, and phonological working memory, most of which have not been previously tested in individuals who had thiamine deficiency in infancy. The twin who had thiamine deficiency showed selective deficits in various language domains, including syntactic movement, morphology, and lexical abilities (which also caused surface dyslexia in reading aloud). She also showed impaired input and output phonological working memory and impaired reading aloud of nonwords (involving voicing errors, morphological errors, and lexicalizations). Her twin sister, who did not have thiamine deficiency, showed typical language abilities. The findings show for the first time that language disorders due to thiamine deficiency in infancy persist into adulthood. In light of previous literature of adults whose thiamine deficiency took place in adulthood, who do not show language impairments, we suggest that thiamine is crucial for language development during the critical period for first language acquisition in the first years of life. Thiamine deficiency during the critical period may cause long-lasting impairments in syntax, morphology, reading, phonological working memory, and lexical abilities.

1. Introduction

In 2003, 20 Israeli infants were hospitalized with severe neurological symptoms. It was discovered that they all consumed the same type of soy-based milk-substitute baby formula of the brand ‘Remedia’, manufactured by ‘Humana’ (Fattal-Valevski et al., 2005). An analysis of the contents of the formula revealed that the formula had been altered 5 months earlier, and vitamin B1, thiamine, was removed from it (even though it was still stated on the box that the formula contains thiamine). It is estimated that during these 5 months the formula was consumed by approximately 600–1000 infants. The terrible outcomes of this deficiency included the death of three infants due to cardiomyopathy, and the death of another two children years later from complications. Many other children suffer from various problems, mostly neurological impairments, such as epilepsy, ataxia, psychomotor retardation, hearing loss, and

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https://doi.org/10.1016/j.jneuroling.2021.101042
Received 8 March 2021; Received in revised form 9 November 2021; Accepted 9 November 2021
Available online 18 December 2021

swallowing difficulties (Fattal, Friedmann, & Fattal-Valevski, 2011). Previous studies revealed that children who had consumed the deficient formula for at least a month demonstrated language impairments later, even if they had not shown neurological symptoms during the period of consumption and were considered "asymptomatic". Twenty children who had consumed the thiamine-deficient formula were tested by Fattal-Valevski et al. (2009) when they were 2–3 years-old. They were found to have impairments in language production and comprehension compared to their aged-matched peers. Fattal et al. (2011) assessed in more detail the language abilities of 59 of the children when they were 5–7 years old, and found that 57 of them, 97%, had syntactic impairments or difficulties with lexical retrieval. Specifically, the authors reported that most of the children (80%) had a problem in the production and comprehension of structures involving syntactic movement (a disorder called "syntactic SLI/DLD"). Importantly, the children showed normal conceptual abilities and normal IQ, which indicates that the impairment was specific to language, and did not span to general conceptual skills. Further assessment when the children were in second grade (Fattal, 2014; Fattal, Friedmann, & Fattal-Valevski, 2012) revealed again severe language outcomes: of the 61 children tested, 90% had syntactic impairments and 59% had lexical retrieval impairments. Differences were found between the different domains of language: whereas the syntactic impairment of these children persisted, lexical retrieval has improved: of the 36 children who were tested twice – at age 5 and then again at age 8–9, 34 children showed impaired lexical retrieval at age 5–7, but only 22 of them still showed lexical impairments at age 8–9; in contrast, the syntactic deficit was identified in 30 of the 36 five-year-olds, but when they were tested again at age 8–9, 32 of them showed a syntactic deficit. It seems, therefore, that whereas the lexical impairment improves as the children grow, the syntactic deficit remains through childhood. An additional domain that was found impaired is reading, as dyslexia was found in as many as 96% of these children when they were tested in grades 1-3 (Spektor, 2012).

In the current study we examine whether the langauge difficulties reported in childhood persist to early adulthood. We tested a 17 year-old young adult who consumed this formula in infancy, and examined what characterizes her impairment in various domains of language as a young adult. Very special circumstances allowed us to compare her performance to a minimally-different participant who has not consumed the thiamine-deficient formula: her twin sister.

1.1. On thiamine and its crucial neurological roles

Why does thiamine deficiency in infancy lead to such consequences? The crucial roles of thiamine in brain development shed some light on this question. Thiamine, or B1, was the first B vitamin to be identified. As many other vitamins, thiamine cannot be synthesized in the mammalian body, therefore, it must be consumed through dietary sources such as whole-grain cereals, vegetables, nuts, peas, sunflower seeds, beans, meat, poultry, fish, and soybeans (Nazir, Lone, & Charoo, 2019; Whitfield et al., 2018). Thiamine is not stored for the long term in the body and if it is not consumed for 3 weeks, it is depleted. Thus, malnutrition or nutrition lacking essential sources of thiamine for 3 weeks or more may cause thiamine deficiency. A thiamine deficiency-related disease in adults, called beriberi, was already reported in 1630, and thiamine deficiency was identified as the cause of this condition in 1926 (Haas, 1988). Wernicke-Korsakoff syndrome, and its acute phase, Wernicke's encephalopathy, which is thiamine deficiency that is manifested in the central nervous system, was described already in the 1930's. Symptoms include memory loss - mostly anterograde and retrograde amnesia, ataxia, oculomotor abnormalities, aphonia, loss of vibratory sensation, decreased reflexes, loss of coordination, and mental confusion (Kril, 1996; Thomson et al., 2008; Zak, Burns, Lingenfelser, Steyn, & Marks, 1991). Wernicke-Korsakoff syndrome is mostly associated with chronic alcoholism, but can also be found in other diseases that cause impaired nutrition, and is caused by insufficient dietary intake of thiamine, reduced absorption of the vitamin, or depletion of stores in the liver (Butterworth, 1989; Butterworth, Kril, & Harper, 1993; Kril, 1996). As we will discuss further later, thiamine deficiency causes different effects in infants compared to adults, and there is evidence that the infant brain is more vulnerable to lack of thiamine (Butterworth et al., 1993).

As for the mechanisms responsible for thiamine deficiency related diseases, the active form of the vitamin - Thiamine Pyrophosphate (TPP) acts as a coenzyme in the activity of three enzymes that are essential for the cerebral metabolism of glucose: pyruvate dehydrogenase complex, alpha-ketoglutarate dehydrogenase complex, and cytosolic transketolase. In the developing brain, the metabolic processes requiring these enzymes are essential for the synthesis of lipids and nucleotides. Thiamine deficiency, hence, causes a reduction in the activity of those enzymes (Bâ, 2005; Fattal-Valevski, 2011; Haas, 1988). In addition to its co-enzymatic function, thiamine has an important structural role as well, specifically in the developing nervous system, and postnatal thiamine deficiency damages hippocampal cells structurally in the rat - with processes such as axonal growth, synapse formation, and myelogenesis vulnerable to postnatal thiamine deficiency (Bâ, 2005, 2008). Although thiamine-deficiency-related diseases have been known for decades, they remain a worldwide problem in present days: in developing countries mostly due to low-in-thiamine nutrition, and in developed countries due to alcoholism (Barennes, Sengkhamyong, René, & Phimmasane, 2015; Cerroni et al., 2010; Doung-Ngern, Kesornsukhon, Kanlayanaphotporn, Wanadurongwan, & Songchitsomboon, 2007; Haas, 1988).

Thiamine deficiency in infancy is common in polished-(white)-rice-feeding countries, and in countries where thiaminase-containing food are consumed (betel leaf, fermented fish). It is usually found in breast-feeding infants who consume thiamine-deficient breastmilk. Outbreaks of beriberi were reported in recent years in Laos (Barennes et al., 2015; Khounnorath et al., 2011), Thailand (Doung-Ngern et al., 2007), Brazil (Cerroni et al., 2010), India (Bhat et al., 2017), and many other places (Adamolekun & Hiffler, 2017; Coats et al., 2012; Duce et al., 2003; Nazir et al., 2019).

Given the essential roles of thiamine in various processes in the human brain, and its importance during brain development, its effects are broad and severe. Therefore, an examination of the various facets of the effects of its deficiency in infancy is vital. Here we focus on the effects of thiamine deficiency in infancy on language in young adults. We examine in detail its effect on various language abilities.

1.2. Thiamine deficiency and language

A crucial point regarding thiamine deficiency is that it has different effects on language abilities depending on the life period in which the deficiency took effect. Korsakoff's syndrome in adults seems not to affect language, but rather general cognitive and executive functions (Fujiwara, Brand, Borsutzky, Steingass, & Markowitsch, 2008; Oscar-Berman & Evert, 1997; Van Oort & Kessels, 2009). Studies assessing lexical and semantic abilities in individuals with Korsakoff's syndrome, whose thiamine deficiency took place in adulthood, found that their lexical retrieval was intact (Cermak, 1976; Cermak & Moreines, 1976; Cermak, Reale, & Baker, 1978), and only conceptual-semantic abilities, non-specific to language, were impaired. There are also no reported syntactic impairments in adults with Wernicke's encephalopathy or Korsakoff's syndrome, nor other specific language impairments, and though they show memory difficulties – including when they have to remember lists of words – these patients show good performance on the vocabulary parts of the WAIS test (Butters, Cermak, & Brown, 1980; Mair, Warrington, & Weiskrantz, 1979). One study that did report a case of a Korsakoff's patient with "confabulation within the sphere of language" also states that "grammar and syntax are formally correct and there is no real nominal aphasia" and concludes that the problem might be conceptual rather than linguistic ("disorganization of the thought processes") (Clarke, Wyke, & Zangwill, 1958).

Children with Fetal Alcohol Spectrum Disorders (FASD) and specifically Fetal Alcohol Syndrome (FAS), who were exposed to alcohol prenatally, often do show language impairments (Church, Eldis, Blakley, & Bawle, 1997; Coggins, Timler, & Olswang, 2007; Wyper & Rasmussen, 2011). It was reported that these children performed significantly below the controls on language tasks (Abkarian, 1992; McGee, Bjorkquist, Riley, & Mattson, 2009), and that whereas younger children (4;0–8;11) had a more global language impairment, older children (9;0–12;11) had an impairment specific to syntax (Carney & Chermak, 1991). Moreover, the language impairments in individuals with FAS may persist into adulthood (Andrade, Fisberg, & De Micheli, 2013). At least some symptoms of FASD are suspected to be related to thiamine deficiency (Bâ, 2008, 2017; Roecklein, Levin, Comly, & Mukherjee, 1985), however many individuals with FAS also show hearing loss and epileptic seizures (Bell et al., 2010; Church et al., 1997), which, in turn, were shown to be related to specific language impairments (Delage & Tuller, 2007; Friedmann & Szterman, 2006, 2011; Monjauze, Tuller, Hommet, Barthez, & Khomsi, 2005; Shalom, 2020), so the language impairments in this syndrome may result from reasons other than thiamine deficiency.

1.3. The present study

In this study we administered a comprehensive assessment of syntax, morphology, lexical retrieval and learning, reading, and verbal memory of two non-identical twin sisters, one of whom had consumed the thiamine-deficient formula (she was 1;0–1;5 during the time the formula was deficient in thiamine), and the other had consumed a milk-substitute with sufficient amount of thiamine. These unique circumstances enable a comparison between two individuals who grew up in a similar environment, and had very similar exposure to language, but minimally differed in whether or not they consumed thiamine.

The current study has three main goals: First, it aims to characterize in detail the language impairments of an individual who had thiamine deficiency in infancy, by examining a range of language abilities, most of which have not been previously examined in individuals with thiamine deficiency, such as reading, lexical learning and encoding, morphology, and phonological working memory.

Second, as language was previously only assessed in this deficiency in children, this study is the first to assess language in this deficiency in adults. This allowed us to shed light on an open question about the critical period for language acquisition, as well as mechanism by which thiamine deficiency affects language. As discussed above, the findings from children with thiamine deficiency due to consumption of the thiamine-deficient formula show that thiamine deficiency in infancy causes language impairments in childhood. In contrast, adults with Korsakoff's syndrome, also caused by thiamine deficiency, but in adulthood, do not show language impairments. The current study allows us to adjudicate between two hypotheses: It might be that thiamine deficiency affects language only in children, but not in adults; in this case we would expect that the language impairments found in the children who consumed the thiamine-deficient formula will not persist to adulthood. Alternatively, thiamine deficiency may have different effects depending on timing of the deficiency itself: when thiamine deficiency takes place during infancy, it results in language impairments, but when it occurs only in adulthood, it does not affect language; in this case we would expect that individuals who had thiamine-deficient nutrition during infancy will have long-lasting language impairments, that will persist into adulthood. Testing a young adult who had thiamine deficiency in infancy will help in deciding between these possible reasons. Is thiamine deficiency *per se* the reason for the language impairments found in the children who were fed with the deficient formula, or is the specific period in which the thiamine deficiency occurs leads to different consequences?

Finally, our study method allowed us to reduce the effect of differences in linguistic input on language acquisition by testing twins who grew up in a similar environment, one of which had consumed a thiamine deficient formula in infancy, and the other had not.

2. Method

We tested the twins in three sessions, each of 2–3 hours. The twins were tested simultaneously by the three authors, in two separate rooms, and the sessions were recorded for later analyses. Tests of different skills (e.g., syntax, reading, lexical retrieval) were administered in a mixed order. The twins and their mother signed an informed consent prior to testing, and were informed that they can take as many breaks as they want during the sessions and can stop their participation at any time. The study was approved by the Tel Aviv University ethics committee.

2.1. Participants

2.1.1. Adi and Hadas

Adi and Hadas are non-identical twin sisters, who were tested when they were 16;9–17;1 years-old. Whereas Hadas had consumed the regular dairy formula that contained sufficient amount of thiamine, Adi had some digestive issues as a baby, and therefore her parents replaced her dairy formula with a more expensive, soy-based formula from the same brand, which later turned out not to include thiamine.

2.1.1.1. Adi. Adi had consumed the soy-based baby formula since she was 0;6 until she was 1;5; as the formula has become thiamine-deficient when she was 1;0 year old, we estimate that she has been consuming the thiamine-deficient formula for five months. Her mother reports that her nutrition, albeit not very common for infants after age 1 year, was only the thiamine-deficient formula without other sources of thiamine. When she was 3-4 years old, Adi's language impairment was evident. She therefore went to a "language kindergarten" – a special education kindergarten that specializes in language difficulties – and was also treated by a speech-language pathologist during her years in kindergarten.

After kindergarten (where she stayed an additional year), throughout her years at school, she studied in special classes for children with learning difficulties and behavioral disorders with a small number of students. The small number of students in these classes allows for more attention and personalized teaching compared to students in regular classes. At the time this study was conducted, Adi was in the 10th grade. She reports difficulties in learning and doing her homework, and states that she is able to read by herself but struggles to understand what she reads. Adi also reports that she feels different from other children her age. Although she had difficulties with many of the tasks during our assessment, Adi was able to stay focused for long periods of time and was very cooperative and motivated during the meetings.

2.1.1.2. Hadas. Hadas, the twin sister of Adi, consumed the dairy baby formula of the same brand, 'Remedia', which was not thiamine-deficient. Her mother reports that Hadas started speaking relatively late, at around age 2;6, but quickly caught up without intervention.

At the time of testing, Hadas was studying in a regular 11th grade class. She did not report any difficulties in school or in general. She states that she usually prepares her homework by herself without any difficulty. Hadas has very high academic achievements, and her mother reports that she is an outstanding student. Hadas is very talkative and communicative. During the meetings, she told us that she found the tests easy and unchallenging.

2.1.1.3. Environmental similarities and differences between the twins. Adi and Hadas were raised in the same home and by the same parents, and had very similar interactions with their parents and other family members, including their two younger sisters (who do not have any language difficulties). During childhood, Adi and Hadas shared a bedroom until the second grade, and their mother reports that she used to read stories to the two of them together.

The family members spend time together at home and during frequent family vacations. Adi and Hadas study in separate classes, as mentioned above, due to Adi's difficulty in comprehending the study material at school, therefore they have different friends with whom they meet in the afternoons. They also have different hobbies - Adi enjoys sports, whereas Hadas is interested in fashion. It was apparent during the meetings in the lab that the twins have a lot of interactions with each other and with their mother.

2.1.2. Control groups

We compared the performance of the twins on each task to the performance of a control group whose data were collected as part of the task development in our lab (see Appendix A for information about the control groups for each of the tests[2]). The comparison of each twin to the control group was performed using the Crawford and Howell (1998) t-test.

[2] The twins were compared to control groups of young adults and adults, because young adults at the age of 17 have completed the acquisition of all language aspects tested in the current study and perform comparably to adults in tests administered in the current study (cf. Friedmann & Gvion, 2002, for pWM tasks; Friedmann et al., 2015, for syntactic tasks). We note, however, that in all tests in which Adi was found to perform significantly below an adult control group, she also performed significantly worse than control groups of children younger than her.

3. Assessment: procedures and results

3.1. Syntax

We tested the twins' syntactic abilities using sentence comprehension, production, and repetition tasks that proved sensitive in identifying syntactic difficulties in various populations (agrammatic aphasia, Friedmann, 2001, 2006; syntactic SLI, currently sometimes termed "syntactic DLD", Friedmann & Novogrodsky, 2004, 2007, 2011; Novogrodsky & Friedmann, 2006; and children with hearing impairment, Friedmann & Szterman, 2006, 2011; Szterman & Friedmann, 2014, 2015). The tasks involve sentences derived by syntactic movement, which are known to be difficult for individuals with syntactic SLI (Friedmann & Novogrodsky, 2004, 2007, 2011; Friedmann, Yachini, & Szterman, 2015), and for individuals who had thiamine deficiency in infancy (Fattal et al., 2011; Friedmann, Fattal, & Fattal-Valevski, 2010).

The tasks include sentences with two types of movement: Wh-movement and verb-movement. Wh-movement (also called A-bar movement) derives wh-questions, relative clauses, and topicalization structures. Wh-movement of a phrase across another phrase ("crossing movement"), as in object questions, object relatives, and topicalization, in which the word order in not canonical, is difficult for individuals with a syntactic impairment, more so than wh-movement that does not change the canonical word order (Friedmann et al., 2015). Examples of sentences with crossing wh-movement are given in (1)–(3) below:

(1) Object relative: This is the girl who grandma drew __.

(2) Object question: Which girl did grandma draw __?

(3) Object topicalization (translated from Hebrew): This girl, grandma drew __.

The other type of movement we tested was movement of the verb from its original position after the subject ("Yesterday the fox jumped") to the second position in the sentence following another element ("Yesterday jumped the fox"), a movement that is optional in Hebrew (Shlonsky, 1997; sometimes termed "triggered inversion", or "V-to-C movement"). Difficulty with this kind of verb movement in Hebrew was also reported for individuals with syntactic impairments (Friedmann, 2013; Friedmann, Gvion, Biran, & Novogrodsky, 2006, for agrammatic aphasia; Szterman & Friedmann, 2015, 2017, for a syntactic impairment due to a hearing impairment).

3.1.1. Relative clause comprehension and paraphrasing

3.1.1.1. Procedure. This task (Meguvana, Friedmann, Novogrodsky, & Szterman, 2004) includes 24 written sentences, including 14 object relative clauses, 7 subject relative clauses, and 3 coordinated sentences as fillers. The participant was asked to read aloud each sentence, and then to explain it in her own words. If the participant did not explain explicitly who did what to whom in the sentence, the experimenter asked her specific questions that encourage an explicit explanation.

3.1.1.2. Results. Adi made errors in 8 of the 21 sentences with relative clauses (38%). Most errors (6) occurred when she tried, and failed, to explain object relatives (43% of object relatives), which include crossing syntactic movement. Adi made significantly more errors on object relatives than the control group of 13 Hebrew speakers (who made only 4% errors, SD = 7%, $t(12) = 5.37$, $p < .0001$). Adi's other two errors occurred in subject relatives (29% of subject relatives, all center embedded), also significantly more than controls (7%, SD = 10%, $t(12) = 2.12$, $p = .003$). As for error types, most of Adi's errors resulted in a reversal of the thematic roles in the sentence. For example, when asked to paraphrase the sentence "the witch whom the model pulled stood up", Adi responded: "I

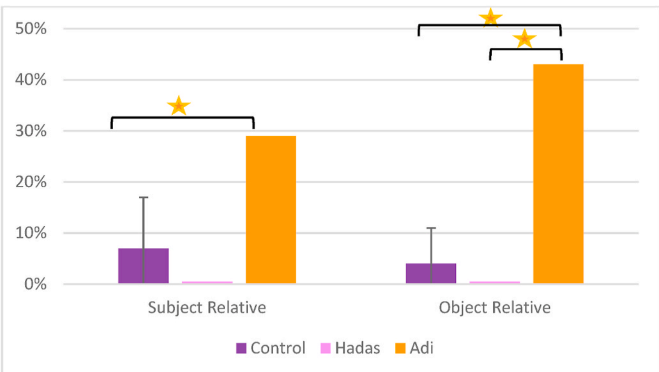

Fig. 1. Percentage of errors of Adi, Hadas, and the control group on the written sentence comprehension task.

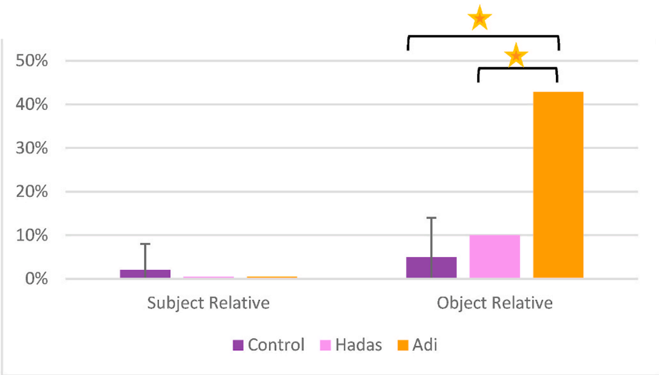

Fig. 2. Percentage of errors of Adi, Hadas, and the control group on the relative clause production task.

didn't understand the sentence myself… the witch pulled the model", the experimenter then asked Adi "who stood up?", and her response was "the model".

Hadas made no errors at all in this task, which is a significantly better performance than Adi in object relatives, Fischer exact p = .008. They did not differ in subject relatives, Fischer exact p = .23. The twins' performance compared to the control group is summarized on Fig. 1.

3.1.2. Relative clause production

3.1.2.1. Procedure. We assessed the twins' production of subject and object relative clauses using a preference task (Adif, BAMBI battery, Friedmann & Novogrodsky, 2004; Friedmann & Szterman, 2006; Novogrodsky & Friedmann, 2006). The participant was presented with 24 short stories about two women, and was asked which of the two women she preferred to be. The participants were asked to begin their answer with the words 'I would rather be … ' in order to encourage the use of relative clauses. Ten of the items elicited subject relatives and 14 elicited object relatives (10 direct object relatives, 4 indirect object relatives).

3.1.2.2. Results. The performance of the twins compared to the controls is summarized on Fig. 2. 43% productions in target object relatives were ungrammatical or non-target responses, significantly more than the control group of 13 young adults (Mean = 5%, SD = 9%, t(12) = 4.07, p = .0008). Her subject relatives, in contrast, were comparable to the controls' (Mean = 2%). Hadas, on the other hand, made only one non-target response in this task (producing a grammatical subject relative with a reflexive verb instead of an object relative), which she immediately corrected, showing a significantly better performance than Adi (Fischer exact p = .04).

Most of Adi's erroneous responses (67%) were ungrammatical sentences (e.g., "I prefer to be that my mother would drive me"). She also produced a subject relative instead of one target object relative.

3.1.3. Sentence repetition

3.1.3.1. Procedure. In this task (PETEL, Friedmann, 2000) the participants were requested to repeat 20 sentences, 15 of which included syntactic movement, and 5 were simple control sentences without movement. The sentences with movement were: 4 object which-questions, 3 object relatives, 3 object topicalization – which all involve crossing syntactic movement and 5 sentences with verb movement. The simple sentences included the same words as the sentences with movement and the same number of words, so they minimally differed from the sentences with movement with respect to whether or not they contained crossing movement.

The participants were asked to count to 3 out loud, before repeating the sentence. Counting was used to prevent rehearsal in the phonological loop (Baddeley, 1997; Friedmann, 2001). Errors in repetition were coded according to the types of errors: structural or lexical. Structural errors involve change in word order or substitution of thematic roles (e.g., This is the musician that the boy admires → This is the musician that admires the boy), and lexical errors involve omissions or substitutions of words with other words that did not occur in the sentence (e.g., Yesterday the boy met the neighbor → Today the student met the neighbor).

3.1.3.2. Results. Adi made 60% errors when she tried to repeat sentences involving object wh-movement, significantly more than the controls (who made only 9% errors on these sentences, SD = 9%), t(12) = 5.20, p = .0001, and 60% errors on sentences involving verb movement, also significantly more than the controls (who made 6% errors on these sentences, SD = 10%, t(12) = 5.46, p < .0001). In contrast, Hadas performed within the norm, with 20% errors on sentences involving object wh-movement and verb movement, which is not significantly different from the control group (t(12) = 1.18, p = .13), and significantly better (fewer errors) than her sister's (Fischer exact p = .03). The twins' performance compared to the control group is summarized in Fig. 3.

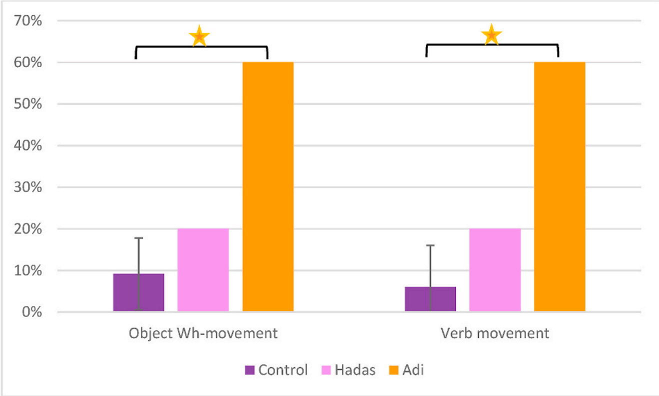

Fig. 3. Percentage of errors of Adi, Hadas, and the control group on the sentence repetition task.

As for error types, three of Adi's errors were structural errors (e.g., she repeated the topicalized sentence: "this teacher, the student was looking for", as "This teacher was looking for the teacher"), five errors were purely lexical (e.g., "This is the student who the teacher was looking for" was repeated as "This is the girl who the teacher was looking for"), and the remaining three errors included both structural and lexical changes of the target sentence. Hadas only made 3 errors, all of which were structural errors.

3.1.4. Interim summary – syntax

In the syntactic tests, whereas Adi, the twin who had had thiamine deficiency, showed consistent difficulty in syntactic movement, Hadas' performance was very good and similar to the controls on all tests.

Adi made significantly more errors than the control group in comprehension, production, and repetition of sentences involving syntactic movement – relative clauses, structures with verb movement, wh-questions, and topicalization. Her difficulty was most severe in structures in which the canonical word order of the sentence is changed, which were shown to be most difficult for individuals with syntactic SLI (Friedmann & Novogrodsky, 2004, 2007, 2011; Friedmann et al., 2015) and to deaf and hard-of-hearing children and adults who were not exposed to sufficient language input early in life (Friedmann & Szterman, 2006; Szterman & Friedmann, 2003). A similar difficulty with syntactic structures involving syntactic movement was reported for the majority of the children who consumed the thiamine-deficient Remedia formula when they were 5-years-old (Fattal et al., 2011), and remained when the children where 8-9 years-old as well (Fattal, 2014). We recently tested eight of the children again when they were 16–17-years-old, and found that all tested children still showed a similar syntactic impairment (Katz, Haluts, & Friedmann, 2019). In contrast, Adi's twin Hadas, who did not have thiamine deficiency, did not show any difficulty with any of the syntactic structures, and her performance was comparable to the control group.

3.2. Morphology

We tested the twins' inflectional and derivational morphology in verbs using a sentence completion task.

Semitic languages, including Hebrew, have non-concatenative morphology. This means that most inflectional and derivational morphemes are not linearly stringed to the root, but rather discontinuously modify it. The Semitic root is understood in classical grammars as an ordered set of consonants (usually three) that denotes a general semantic field. A specific denotation and a phonological realization is attained only when the root letters are inserted in a morphological template/pattern.

Each verb in Hebrew is derived in one of five patterns (CaCaC, CiCeC, niCCaC, hitCaCeC and hiCCiC[3]). For example, the root lmd refers to the general semantic field of learning, and can generate the verbs *lamad* – 'learned, studied' in the CaCaC pattern, *limed* – 'taught' in the CiCeC pattern, and *hitlamed* – 'apprenticed' in the hitCaCeC pattern. Each verb is also inserted in an inflectional template, marking tense and agreement with the subject (in person, gender, and number).

The morphological task examined inflectional morphology, including tense and agreement, and derivational morphology of verbal patterns, especially intransitive-transitive pairs (e.g., *nisgar, the intransitive* 'closed', and *sagar, the transitive* 'closed'; *rakad* – 'danced', and *hirkid* – 'made someone dance').

3.2.1. Sentence completion

3.2.1.1. Procedure. In the sentence completion task (Hišlim, from the HIFIL test battery, Katz & Friedmann, 2020), the experimenter read 48 sentences, each sentence was missing a verb. The participant could follow the printed text if she found it helpful. The first part of the sentence contained a verb that is one member of an intransitive-transitive pair, presented in bold and read by the examiner with

[3] C represents root consonant slots, and other symbols represent consonants and vowels that are part of the pattern.

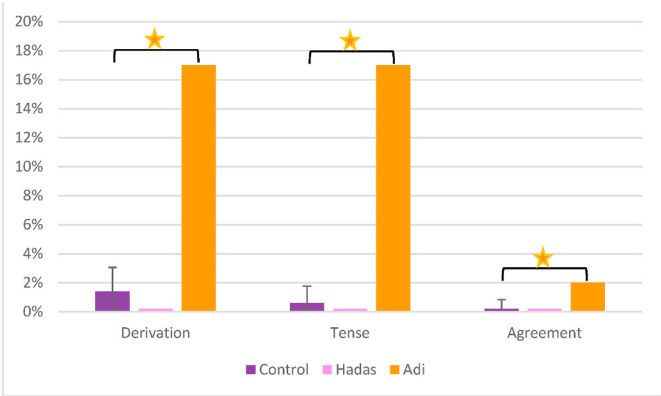

Fig. 4. Percentage of three kinds of morphological errors made by Adi, Hadas, and the control group on the production of the target verbs in the Hišlim task.

prosodic stress. The participant was asked to complete the sentence, and was told that the missing word is related in some sense to the stressed word. The participant was expected to produce the other member of the verb pair, which has the same root but different derivational morphology (a different pattern) and different inflectional morphology (different tense and agreement). In example (4), the given verb is *nidleka*, which is in the niCCaC pattern and with feminine agreement, and the target verb is the causative *hidlik*, which shares a root with the given verb (dlk), but is in the hiCCiC pattern and in masculine inflection.

(4) Ha-menora ba-salon nidleka ki Uri laxac

The-light$_{.FEM}$ in-the-living-room turned-on$_{Intr.FEM}$ because Uri($_{MASCULINE}$) pressed$_{.MASC}$ al ha-meteg ve-__ ota. on the-switch and-_ her. (Target: *hidlik* – 'turned-on$_{Tr.MASC}$')

"The light in the living room turned on, because Uri pressed the switch and turned it on"

3.2.1.2. Results. The performance of Adi and Hadas compared to the control group is summarized in Fig. 4. Adi made errors in both derivational and inflectional morphology. She made a total of 8 derivational errors (17% of the items), in which she selected the incorrect pattern for the root. In most of these cases, this resulted in an existing verb (e.g., hitrašem, 'to be impressed' → niršam, 'sign up'; histarka, 'comb$_{Reflexive}$' → sirka, 'comb$_{Tr}$'), but in one case the error resulted in a non-existing combination of root and pattern (raxac, 'wash' → hirxic, non-existent verb in the hiCCiC pattern). Adi made significantly more derivational errors than the control group (which made only 1% errors on average, $SD = 2\%$, $t(20) = 8.98$, $p < .001$).

As for inflectional errors, Adi made eight (17%) tense errors (e.g., do'eg, 'worry$_{PRESENT}$' → da'ag, 'worry$_{PAST}$') and one (2%) gender agreement error (hirgiza, 'irritate$_{FEMININE}$' → hirgiz, 'irritate$_{MASCULINE}$'). She made significantly more errors than the control group in both tense (control $M = 1\%$, $SD = 1\%$), $t(20) = 13.40$, $p < .001$, and agreement (control $M = 0\%$, $SD = 1\%$), $t(20) = 2.92$, $p = .004$. Hadas, in contrast, made no errors at all in this task.

3.3. Reading

We assessed the reading abilities of the twins using several reading tasks, including reading aloud and silent reading of words of different types. The twins' reading is interesting on its own, since, to our knowledge, only one study in the past investigated the effects of thiamine deficiency on reading (Spektor, 2012). Their reading abilities are also highly relevant for the understanding of their language abilities: since reading and language processes share cognitive modules, the twins' performance in reading may help us pinpoint the functional locus of their language impairment, and vice versa (Gvion & Friedmann, 2016). In all of the reading tasks we report here, the participant is presented with a list of words, nonwords, or word-pairs written on a page one above the other, and is requested to read them as quickly and accurately as she can.

3.3.1. Reading aloud single existing words

3.3.1.1. Procedure. We assessed reading aloud of single words using three word-reading tests. The first was the single word screening task from the Tiltan Battery for the diagnosis of dyslexias in Hebrew (Friedmann & Gvion, 2003) – which is a "wide-range" task, developed to identify the various types of known dyslexia by using words that are sensitive to all types of dyslexias in Hebrew (136 words).

We then tested her reading using tests from the Tiltan battery for specific types of dyslexia: the potentiophones task – which contains 78 words sensitive to surface dyslexia. These are words that, when read via the sublexical route rather than via the lexical route, may be read as other existing words (a relevant example in English is "phase" which, if read sublexically to rhyme with "case", would yield "face"; or "none", which, if read sublexically may be pronounced like "known", Friedmann & Lukov, 2008, 2011; Gvion & Friedmann, 2016.

The third word-reading task was the migratable words task – which contains words sensitive to Letter Position Dyslexia (LPD, 120 words). These are words that, when read with a letter position error, i.e., a migration of the middle letters, create other existing words (relevant English examples include slime-smile, beard-bread, signs-sings, Friedmann & Gvion, 2001; Kohnen, Nickels, Castles, Friedmann, & McArthur, 2012).

3.3.1.2. Results. We compared the performance of the twins to the performance of 944 adults in the single word screening test, to 372 adults in the potentiophones task, and to 452 adults in the migratable words task.

Adi's reading pattern indicates that she has surface dyslexia – a deficit in the lexical route that forces her to read existing words using grapheme-to-phoneme conversion (Castles & Coltheart, 1993; Coltheart, Masterson, Byng, Prior, & Riddoch, 1983; Marshall & Newcombe, 1973). This deficit in the lexical route causes regularizations and phonologically plausible misreadings of words, which in Hebrew is especially pronounced due to the large degree of freedom in reading via the sub-lexical route.

In the single-word screening task, Adi made errors in 25 of the words, 20 of these were surface errors (15% of the target words). She also made two voicing errors (2%), and two morphological errors. Hadas, in contrast, did not make any errors in this task.

In the potentiophones task, in which all words are sensitive to surface dyslexia, Adi made a total of 23 errors, 21 of them were surface errors (27% of the target words). The number of surface errors Adi made in these tests was significantly above the norm (single word screening, the norm for adults is $M = 1.1$, $t(943) = 14.9$, $p < .001$, potentiophones: $M = 3.71$, $SD = 2.70$, $t(371) = 6.76$, $p < .001$).

In the migratable words task, Adi did not make any letter transposition errors, even though the task includes stimuli sensitive exactly to this type of errors (and even though letter position dyslexia is very common in Hebrew readers). She did make 17 errors in this task, 15 of them were surface errors (significantly more surface errors than the norm, $M = 1.82$, $SD = 1.51$, $t(451) = 8.73$, $p < .0001$), and 2 were voicing errors.

Hadas made 7 surface errors in the potentiophones task, and 3 letter transpositions in the migratable words task, both within the norm (potentiophones: $t(371) = 1.22$, $p = .11$; migratable: transpositions – M control = 1.46, $SD = 1.55$, $t(452) = 0.99$, $p = .16$). She did make significantly more surface errors than the controls on the migratable words task ($t(451) = 2.10$, $p = .02$), however – because all of these errors were done when she read at a relatively fast pace and were immediately self-corrected, and because she did not make more surface errors than the norm on any of the other tests, including the potentiophones task which is sensitive specifically for this type of errors, we conclude that Hadas' reading is intact.

Most of Adi's errors in reading single existing words occurred in potentiophones, which are most sensitive to surface dyslexia, supporting our conclusion that Adi's main deficit in reading words was a deficit in the lexical route.

3.3.2. Reading aloud word pairs

3.3.2.1. Procedure. To test whether the twins have attentional dyslexia, causing migration of letters between neighboring words (Friedmann, Kerbel, & Shvimer, 2010; Shallice & Warrington, 1977) we used the word-pair task from the Tiltan screening test (30 word pairs), and the "Kishbiyon" task for attentional dyslexia (32 pairs) from the Tiltan Battery (Friedmann & Gvion, 2003).

3.3.2.2. Results. Adi did not make any attentional errors in either of the word-pair reading tasks. She did make surface errors in these tasks. In the screening word-pair reading task Adi made 5 surface errors (8%), significantly more surface errors than the control group of 978 adults ($M = 1.3$, $t(977) = 2.7$, $p = .004$). In the Kishbion task as well, Adi made mostly surface errors - 6 (9%), again significantly more than the control group of 443 adults ($M = 0.4$, $SD = 0.7$, $t(42) = 7.91$, $p < .0001$).

Hadas, on the other hand, made only one error in the word-pair reading task, and 3 errors in the kishbion task – 2 migrations between words and one surface error, which is within the norm for these tasks.

These results show that Adi has no attentional dyslexia, and support our claim that she has surface dyslexia.

3.3.3. Reading aloud nonwords

3.3.3.1. Procedure. In order to assess the twins' ability to use the sublexical route that converts letters to phonemes, we tested their reading aloud of nonwords using the nonword screening task (40 nonwords) and the "Cylkiyot" task (41 nonwords) from the Tiltan battery (Friedmann & Gvion, 2003). The "Cilkiyot" task, which involves reading of morphologically-complex nonwords, is specifically aimed to test the participant's ability to read the word in an existing morphological pattern. Since Hebrew orthography underspecifies some of the vowels in the middle of the word, and a lot of the information about the vowels in the word is derived from the morphological structure of the word, the reader has to use her morphological knowledge in order to analyze the morphological structure of the word and read the nonword correctly. For example, the letter string CLKIOT in Hebrew can be read as "cilkiyot" (similarly to *pitriyot* - 'mushrooms'), "calakiyot" (similarly to *kalaniot* –'anemones') and "calkiyot" (similarly to *xarciot* – 'chrysanthemums'), but not as "calakayot", "calakayavat", "cilekiyot", "cilikiyot" etc., because these renderings do not correspond to the vowel pattern in any Hebrew morphological pattern. The morphological pattern is converted from orthography to phonology in a dedicated route (Friedmann & Coltheart, 2017, 2018), and merged with the root letters, read via the lexical or the sublexical route in the phonological output buffer.

3.3.3.2. Results. In the nonword screening task, Adi made 5 errors, all of which were lexicalizations– she read the nonword as an existing word: 4 consonant transpositions in migratable nonwords, which is significantly more than the number of transpositions in the control group of 883 adults ($M = 0.9$, $SD = 1.1$, $t(882) = 2.82$, $p = .002$), and one consonant substitution.

Of the 41 morphologically complex nonwords in the "Cilkiyot" task, Adi read only 29 (71%) in an existing derivational pattern (namely – she read the morphological templates in a phonologically plausible way which did not correspond to any existing morphological pattern), which is significantly below the control group of 40 adults (mean = 89%, SD = 7, $t(39) = 2.54$, $p = .008$). She also made 4 voicing errors, 1 transposition, and 1 morphological error (the control group made none).

Hadas made no errors in the nonword screening task, and only one (transposition) error in the "Cilkiyot" task, so her performance was within the norm also for nonwords.

Whereas Adi did not make any transposition errors in existing words, suggesting that she does not have LPD, nor did she make transposition errors in existing words or in nonwords in which a transposition does not create an existing word, she did make transpositions in migratable nonwords when these resulted in lexicalization. As we will show later, these transpositions in migratable nonwords resulted from her phonological output buffer deficit.

These results also indicate that Adi has some difficulty in reading words according to existing morphological forms in Hebrew, this applies both to morphologically complex words and to morphologically complex nonwords, and indicates that she was using the grapheme-to-phoneme conversion route instead of a dedicated route for converting the orthographic form of whole morphological affixes to their phonological representations. The data also show a consistent deficit in the conversion of the voicing feature, which was more pronounced in reading nonwords than in word reading, and occurred also in reading words but only in words read sublexically. These voicing errors may result either from a deficit in voicing conversion in the sublexical route (as in Gvion & Friedmann, 2010) or from a deficit in the phonological output buffer.

3.3.4. Lexical decision and word association tasks

Adi's reading aloud showed very clear indications of surface dyslexia. Surface dyslexia may result from deficits in different components in the lexical route (Coltheart & Funnell, 1987; Friedmann & Lukov, 2008, 2011; Hanley, 2017; Kohnen et al., 2018). To determine whether Adi's surface errors originate from an impairment to the orthographic lexicon, which stores the written form of words known to the reader, or from a deficit in a later stage in the lexical route, we used tasks that involve the orthographic lexicon, without the later phonological output stages.

The first task was a lexical decision task, in which the participant was presented with 22 pairs of a word and its pseudohomophone – a nonword that can sound the same when read through the sublexical route (city-sity). The participant was requested to circle the existing word ("the word that is written correctly"). In this task Adi had perfect performance, 100% correct.

The second task was a written homophone/potentiophone association task, in which Adi was presented with 40 pairs of written potentiophonic or homophonic words, and a third word that is semantically related to one of them (a relevant example in English would be 'question' presented with 'which' and 'witch'). The participant was asked to decide which member of the pair was related to the third word. Adi showed very good performance on this task too. She made only one error in this task (2.5%), which is not different from the control group (M = 0.67 errors, SD = 0.94, $t(140) = 0.35$, $p = .36$).

3.3.5. Interim summary – reading

Whereas Adi's word and nonwords reading was impaired, Hadas' reading was very good and within the norm on all reading tasks.

Adi's performance was characterized by many surface errors in reading words aloud; in nonwords she made lexicalizations and voicing errors. She did not make letter transposition errors in real words, nor did she make errors characteristic of attentional dyslexia or vowel dyslexia (although these dyslexia types are 3 of the 4 most common types in Hebrew, Khentov-Kraus & Friedmann, 2016; Friedmann & Coltheart, 2018).

Surface errors result from reading via the sublexical route, rather than via the lexical route. Adi's lexical decision and comprehension of written homophones, which were good and within the norm, indicate that her orthographic input lexicon is intact, so her deficit in the lexical route has to result from a deficit in later stages in the lexical route. As we will report below, her lexical retrieval was impaired as a result of a phonological output lexicon deficit. We suggest that this deficit in the phonological output lexicon was also the origin of her surface dyslexia, forcing her to read aloud via the sublexical route. (For a discussion of types of surface dyslexias and their relation to lexical retrieval see Friedmann & Lukov, 2008; Gvion & Friedmann, 2016.)

Adi's good performance in the homophone comprehension task also indicates that her conceptual abilities are intact. In order to succeed in this task, the participant must understand the (sometimes abstract) concepts that the words denote and the different kinds of relations between them, and then evaluate two relations and decide which one is stronger. Adi's success in this task shows that she can do that easily, and therefore her conceptual skills cannot be the source of her linguistic difficulties.

As for her transposition errors in nonwords, in general, such errors can either stem from a deficit in the letter position component in the letter position component in the orthographic analyzer (letter position dyslexia, LPD, Friedmann & Gvion, 2001), or from a deficit in the phonological output buffer. We claim that the latter is true in the case of Adi. First, Adi made transpositions only in nonwords, but not in words, even though the word reading tasks included more than 200 real words that are especially sensitive to migrations - migratable words. In fact, she read the migratable word task dedicated to letter position dyslexia, which included 120 migratable words, without a single migration, an achievement of only 16% of the control participants without dyslexia who read this word list (73 of 452 control participants).

Furthermore, all of her transpositions in nonwords were lexicalizations, i.e., the transpositions resulted in real words. The findings that the transpositions occurred only in nonwords and that they resulted in lexicalizations can both be explained by an impairment in the phonological output buffer. Whereas in real word reading, the phonological output lexicon provides support to phoneme strings held in the phonological output buffer, no such support can be provided for nonwords-which leads to more errors in nonword reading and to lexicalizations in individuals with phonological output buffer impairment.

Voicing errors can stem either from an impairment in the grapheme-to-phoneme conversion, or from an impairment to the phonological output buffer. Parsimony suggests that the latter hypothesis is true, because we already have to assume an impairment in the phonological output buffer in order to explain Adi's lexicalizing transposition errors in nonwords.[4] Indeed, we will later show that Adi has low phonological output memory, and that she makes many voicing errors also when repeating nonwords, further supporting the conclusion that her voicing errors stem from her phonological output buffer deficit.

In the next two sections we will discuss Adi's difficulties with phonological working-memory and with lexical retrieval, which we believe to be the source of her difficulties in reading aloud.

3.4. Phonological working memory

The phonological working memory abilities of the twins were assessed using several tasks (FRIGVI battery, Friedmann & Gvion, 2002; BLIP, Friedmann, 2003) that examined the input pWM component (the Phonological Input Buffer – PIB) and/or the output pWM component (the Phonological Output Buffer, POB). The tasks requiring both PIB and POB included span tests that assess serial recall of lists of words and nonwords, and a task that assesses repetition of single phonologically complex nonwords; A task that involves only the PIB (which can be selectively impaired, Shallice & Papagno, 2019) was a word list matching task.

3.4.1. Serial recall spans

3.4.1.1. Procedure. We used three serial recall tasks from the FriGvi battery (Friedmann & Gvion, 2002; Gvion & Friedmann, 2012a, 2012b): basic word span (two-syllable words), long word span (four-syllable words), and nonword span, all including only simple CV/CVC syllables with no complex clusters. The participants heard a list of unrelated words or nonwords, and were requested to repeat the list accurately and in the correct order. Each level contained five lists of the same length (e.g., level 2 contained five lists of two words each). We started on level 2, and moved to the next level if the participant correctly repeated at least 3 lists on a given level. The test ended when a participant correctly repeated less than 3 lists on a level. The memory span was determined by the highest level in which the participant correctly repeated at least 3 lists. Had the participant correctly repeated 2 lists of the 5 on the final level, she received an extra 0.5 point to the calculated span.

3.4.1.2. Results. The performance of the twins was compared to control groups of young adults aged 20–30 (reported in Gvion & Friedmann, 2012a). The recall spans of Adi, Hadas, and the controls are indicated on Fig. 5. Adi's spans were significantly lower than the spans of the controls in all serial recall tests: she had a span score of 3 on the basic word test, $t(135) = 3.59$, $p = .0002$; 2.5 on the long word test, $t(18) = 3.05$, $p = .003$; and 1.5 on the nonword span test, $t(147) = 4.03$, $p = .00004$.

Hadas' performance was good and did not differ from that of the controls on the basic- and long word tests, she had a span score of 5 on the basic words test, $t(135) = 0.57$, $p = .28$, and 4 on the long word test, $t(18) = 0.90$, $p = .19$. Her span on the nonword test was 2.5, which is slightly below that of the control participants $t(147) = 1.77$, $p = .03$.

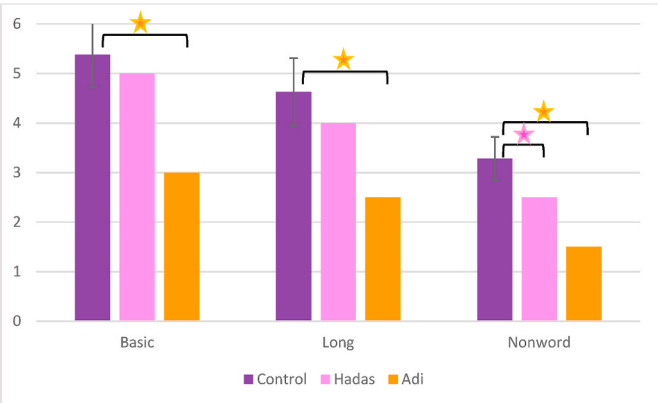

Fig. 5. Span scores of Adi, Hadas, and the control groups on the serial recall tests.

[4] The alternative possibility that Adi's voicing errors in reading and in repetition stem from impairments to the grapheme-to-phoneme and phoneme-to-phoneme conversion routes accounts for the findings in the following way: Her voicing errors in reading were mostly in nonwords and in existing words in which she made surface errors – both indicate reading via the sublexical route and using grapheme-to-phoneme conversion. In repetition, her voicing errors were mostly in the repetition of nonwords, which is performed via the phoneme (input) to phoneme (output) conversion route.

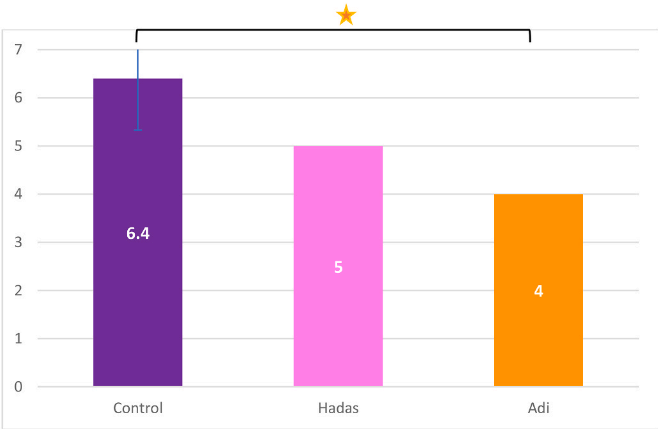

Fig. 6. Span scores of Adi, Hadas, and the control group on the pWM matching test.

3.4.2. *Matching span*

3.4.2.1. Procedure. To assess the twins' PIB separately, without the POB, we administered a matching span test the FriGvi battery (Friedmann & Gvion, 2002; Gvion & Friedmann, 2012a, 2012b): The participants heard pairs of lists of unrelated words, which were comprised of the same words. In half of the pairs the words appeared in the same serial order, and in the other half two consecutive words appeared in a reversed order. The participants were requested to decide whether or not the two lists are the same. Each level contained 10 pairs of lists of the same length (e.g., level 2 contained 10 pairs of lists of 2 words each). We started on level 2, and moved to the next level if the participant responded correctly on the first 4 pairs, or on 7 pairs on a level. Otherwise, we returned to the previous level and completed it. The span was determined by the highest level in which the participant responded correctly on at least seven pairs.

3.4.2.2. Results. The performance of the twins and a control group is summarized on Fig. 6. Adi had a span score of 4 on the matching test, which is significantly lower than the controls', $t(9) = 2.14$, $p = .03$. Hadas completed level 5 on the test, and refused to continue further with this test. Thus, her span score was determined as 5, but might actually have been higher. Nevertheless, even a span of 5 is within the range of the spans of the controls, $t(9) = 1.24$, $p = .12$.

3.4.3. *Repetition of phonologically complex nonwords*

3.4.3.1. Procedure. Another task that assessed the twins' pWM and phonological input and output buffers was a nonword repetition task (BLIP, Friedmann, 2003). The examiner said a nonword, and the participant was asked to repeat it accurately. The task included 48 items of length 2–4 syllables: 24 phonologically simple nonwords (with only CV syllables), and 24 phonologically complex nonwords (containing consonant clusters).

3.4.3.2. Results. Adi repeated correctly only 38% of the nonwords, significantly lower than the control group (20 adults aged 23–48), who repeated correctly 95% of the nonwords on average ($SD = 3\%$, $t(19) = 18.54$, $p < .0001$). Adi's performance was affected by phonological complexity: she repeated correctly 50% of the phonologically simple words, and only 25% of the phonologically complex words (both significantly lower than the controls: simple – $t(19) = 11.22$, $p < .0001$; complex – $t(19) = 11.39$, $p < .0001$).

Her errors in repetition of nonwords consisted of substitutions of consonants and vowels, and omissions of consonants. Notably, we reported above that she made voicing errors in reading aloud, and in nonword repetition she made the same type of error, with 7 voicing errors (Fig. 7).

As indicated on Fig. 8, Adi showed a significant length effect in repetition of the phonologically simple nonwords: she was able to repeat short nonwords of 2 syllables quite well, fewer words of 3 syllables, and it was almost impossible for her to repeat the long, 4-syllable words (where she managed to repeat only one word). The correlation between number of syllables and percentage of Adi's correct repetitions was significant (point biserial $r = -0.51$, $p = .01$). Hadas, in contrast, repeated correctly almost all nonwords (96%), with the same percentage correct of phonologically simple and phonologically complex (both 96%) words. Hadas did not show a length effect (2 syllables: 100%, 3 syllables: 88%, 4 syllables: 100%, $r = 0$, $p = 1$).

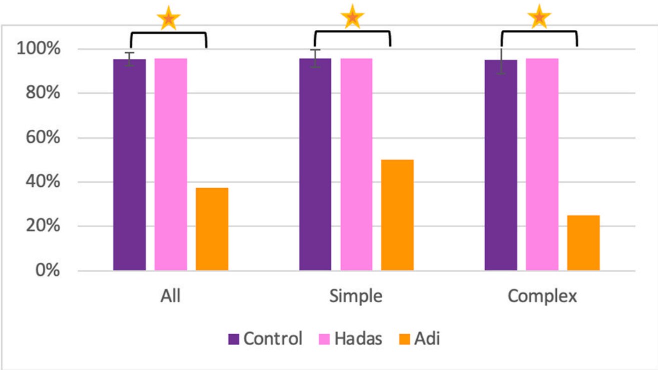

Fig. 7. Percentage of correct responses of Adi and Hadas compared to the control group on the nonword repetition task. Simple – phonologically simple nonwords, Complex – phonologically complex nonwords.

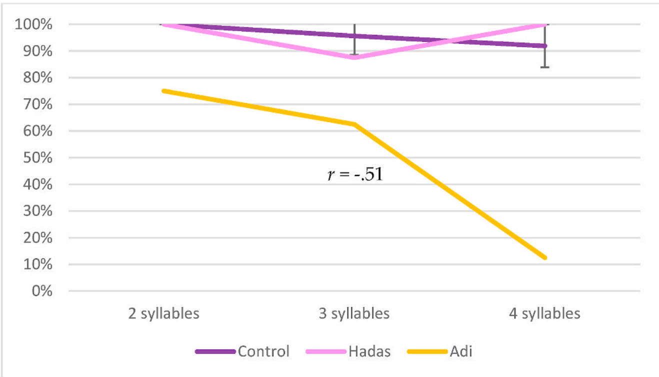

Fig. 8. Percentage of correct responses of Adi and Hadas on phonologically simple nonwords of different lengths.

3.4.4. Interim summary – phonological working memory

Adi showed significantly lower phonological WM spans than the control group in all types of serial recall tasks (basic words, long words, and nonwords), in the task of single nonword repetition, and in the matching span test. Hadas, in contrast, did not show a consistent difficulty in the WM tasks and performed well on all but one of the span tests.

Adi, but not Hadas, also showed a length effect in repetition of single nonwords, which is typical of individuals with pWM impairment (Baddeley, Thomson, & Buchanan, 1975; Dotan & Friedmann, 2015; Hulme & Tordoff, 1989).

A similar impairment was reported for some of the children who consumed the thiamine-deficient formula when they were tested at the age of 8–9 (Fattal, 2014), however – the previous assessment was based on only one task, of repetition of single nonwords. Here we broaden the number and types of tasks, and can conclude that thiamine deficiency in infancy may lead to a pWM impairment, which, in Adi's case, seems to manifest both in the input and in the output pWM mechanisms. The type of errors Adi made in repeating nonwords is typical of impairents to the phonological buffer – omissions of consonants that simplify consonant clusters, substitutions of phonemes, and voicing errors.

Adi's deficit in the phonological output buffer, which is also part of the process of reading aloud, also underlies her deficit in nonword reading, as reported in Section 3.3, and in verb morphology, reported in Section 3.2. Given that she made many voicing errors in nonwords, both in reading and in repetition, we suggest that her voicing errors in reading nonwords stem from the same source, her impaired phonological output buffer).

3.5. Lexical retrieval and word learning

According to the tasks reported above, Adi's conceptual system as well as her semantic lexicon seem to be intact, as indicated by her very good performance on the written homophone association task, and by her good performance in the comprehension of syntactically simple sentences. We continued to test the twins' lexical retrieval using a picture naming task, an irregular plural formation task, a lexical priming task, and a new-word learning task.

3.5.1. Picture naming

3.5.1.1. Procedure. The picture naming task (SHEMESH, Biran & Friedmann, 2004) includes 100 pictures of objects. The participant was asked to name each picture aloud. Responses were coded as correct only when they were the correct object names that were produced within 5 seconds of the presentation of the picture. Erroneous responses were coded according to the type of errors (semantic/phonological/visual/morphological), and as to whether the response followed a long hesitation. We also examined whether a correct response was achieved following a phonological, semantic, or gestural clue that the experimenter provided following a failed retrieval.

3.5.1.2. Results. The performance of the twins was compared to a control group of 86 young adults aged 19–29 (mean of correct immediate naming = 99%, SD = 1.6%). The results of the twins and the controls are indicated on Fig. 9. Whereas Adi was able to immediately name only 85% of the presented pictures, a performance that is significantly lower compared to the control group, $t(85) = 8.87$, $p = .0001$, Hadas named immediately 99% of the pictures, which is comparable to the controls.

Most of Adi's errors (8) were semantic, e.g., she said 'vacuum cleaner' when naming a picture of an iron, and 'hammer' when naming an axe. She also made 3 phonological errors, provided definitions instead of names for 3 objects, and in one case she responded "I don't know".

3.5.2. Plural formation

Plural formation in the nominal domain is mostly regular in Hebrew, with the suffix –im for masculine and the suffix –*ot* for feminine nouns and adjectives. However, there are some exceptions: some nouns undergo a phonological process with the addition of a plural suffix, so that the base morpheme changes phonologically but in a somewhat predictable way (similar to leaf → leaves), some

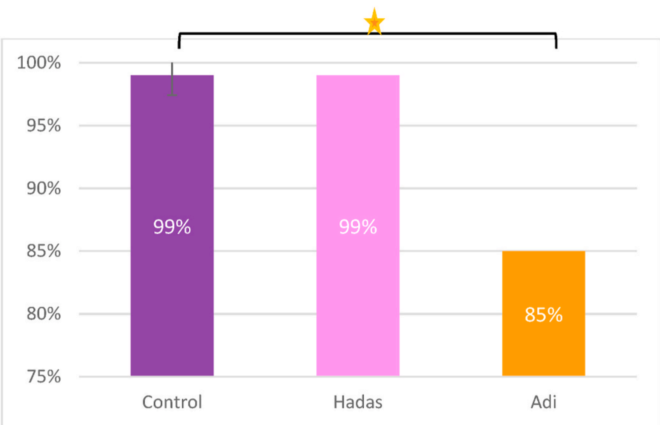

Fig. 9. Percentage of correct immediate naming of Adi, Hadas and the controls (n = 86) on the picture naming task.

nouns receive a suffix that does not regularly match their grammatical gender (i.e., a masculine noun with the feminine suffix *–ot*, or a feminine noun with the masculine suffix *–im*), and some nouns have irregular and unpredictable plural forms (similar to English child → children; mouse → mice). Information about such irregular plurals should be marked in the phonological lexicon, so we tested Adi's plural formation as a way to examine another aspect of her lexical abilities.

3.5.2.1. Procedure. In the plural formation task (Girim, Friedmann, Stark, Rajuan-Gabso, Guggenheim, & Gvion, 2018), the experimenter said the singular form of a noun in a short template ("one X, many/two/three/four__") and the participant was requested to complete the template using the plural form of the noun. The task included 81 items: 20 nouns with regular plural suffixes, 31 nouns that require a phonological process, 27 nouns with a plural suffix that does not match their grammatical gender, and 14 irregular and unpredictable plural forms (e.g., *iš* → *anaš-im,* person-people), seven of the irregular nouns also had a gender mismatch with the suffix.

3.5.2.2. Results. Adi's performance was compared to a control group of 16 adults aged 21–71. Adi made a total of 11 errors in this task (86% correct), a performance that is significantly below that of the control group (which was M = 97.7%, SD = 2.9%, $t(15) = 3.9$, $p = .001$). Five of Adi's errors were in irregular plural forms. In three other cases (two in regular forms and one in a form requiring phonological process) Adi had an error which was lexical/phonological in nature: she produced a plural form of another noun which was phonologically related to the target (e.g., *gir*, 'chalk' → *gargerim*, 'grains'). In two errors in the phonological change condition Adi produced the plural form without the phonological process, in one case she chose the incorrect suffix in the gender mismatch condition, and in one case she did not use a plural suffix and repeated the noun in its singular form.

All these errors indicate that not only base lexical entries but also irregular plural forms that are marked on the lexical entries in the phonological lexicon are impaired in Adi's production.

3.5.3. Lexical priming

3.5.3.1. Procedure. To find the cause of Adi's difficulty in lexical retrieval, we constructed a priming task with pictures. The target words, for both twins, in the lexical priming task were words from the picture naming task that Adi failed to name. Each twin was presented with 10 sets of four pictures of objects; in each set, three of the pictures were used as primes, and the fourth picture was the target. The primes were either semantically related to the target (4 of the sets, e.g., primes: tea, coffee, a cup, target: a kettle), or phonologically related to the target (3 of the sets, e.g., primes: xalil 'a flute', pil 'an elephant', daxlil 'a scarecrow', target: xacil 'an eggplant') or unrelated to it (3 of the sets, e.g., primes: a tree, a flower, a leaf, target: an anchor). The examiner pointed to each of the three primes and named it, and then asked the participant to name the fourth picture (e.g., 'this is a tree, this is a flower, this is a leaf, and what is this?').

3.5.3.2. Results. Adi named correctly 3 of the 4 targets with semantic priming, 2 of the 3 targets with phonological priming, and none of the 3 targets in the unrelated condition, which may indicate that semantic and phonological clues helped her with retrieval. Hadas, in contrast, named all 10 targets correctly and did not make any errors.

3.5.4. Word-learning

3.5.4.1. Procedure. To assess the twins' ability to learn new words, we constructed a word-learning task of words with which we thought the twins would not be familiar, from two categories – flower types and dog breeds. Each twin was presented with 8 pictures of different flowers (e.g., Anemone, Cyclamen, Petunia) and 8 pictures of different dogs (e.g., Poodle, Labrador, Pinscher), with 2–3 syllables. The experimenters taught each of the twins each list separately by presenting the pictures in a fixed order. The participant was asked to name the picture, and if she did not know the name, the experimenter named the picture and the participant was asked to repeat it. After two full presentations of the list in this method, the final two pictures in the list were presented again, interchangeably six times, and the participant was asked to name them again at each presentation. This was done in order to examine whether more extensive exposure to a word will assist Adi in its encoding and retrieval. In this stage as well, when the participant could not retrieve the correct name, the experimenter produced it and the participant repeated it.

There were three assessment points of the full list: at first presentation of the pictures, before we started teaching the words; right after learning, and in the end of the meeting, 2 hours after the learning session.

3.5.4.2. Results. As indicated on Fig. 10, whereas Adi did not know any names of the flowers or dogs in advance (she successfully named 0% of the pictures on the first presentation), Hadas was able to immediately name two of the flowers and two of the dogs (25% of all items). On the second presentation, following the learning session, Adi was able to name only two of the flowers and one of the dogs she has just learned (19%), whereas Hadas named correctly five of the flowers and seven of the dogs (75%). At the final testing point, 2 hours after learning the words, Adi named correctly four of the flowers and one of the dogs (31%), and Hadas named correctly all of the items. Adi showed great difficulty in producing the phonologically more complex words, and made many phonological errors, even when requested to repeat the word right after the examiner said it. For example, she repeated poodle as boodle, labrador as lavroodel, and *karkom* ('Crocus') as kirkom and karkoom. Adi also confused different items with one another, and made between-category errors: e.g., when she was presented with a picture of the flower Petunia at the final testing, she said: "lavroodo, right? … pen … that's a difficult word!", indicating confusion with the dog breed Labrador. Note that Petunia was the last word in the flower list, which was repeated to Adi six more times than other

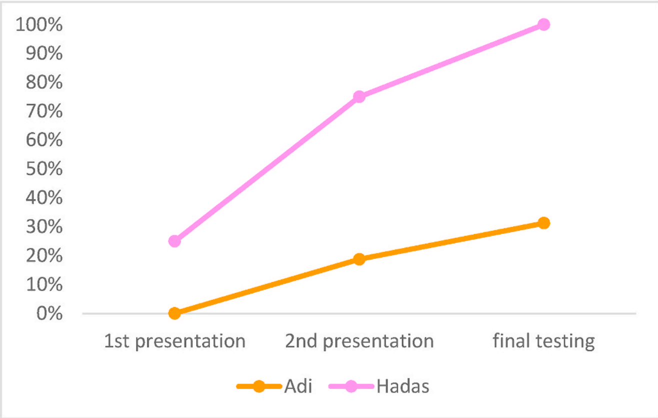

Fig. 10. Percentage of correct responses of Adi and Hadas in the word learning task.

words in the second presentation of the list. It does not seem that the additional exposure helped Adi's retrieval–neither in the case of Petunia, nor in the other three words that were rehearsed 6 more times (in fact, in the two assessment points she could not recall even a single noun from the 4 items that were reharsed 6 more times). Adi was aware that phonologically complex words are difficult for her to produce, and in many cases she tried to correct herself (usually making another error) or to avoid producing the word altogether.

3.5.5. Interim summary – lexical retrieval and word learning

Adi made significantly more errors than the control group on the picture naming task, which suggests she has difficulty with lexical retrieval, whereas Hadas performed comparable to the controls. The fact that both phonological and semantic cues helped Adi in the priming task strengthen our hypothesis that the target words exist in her lexicons, and that her difficulty is indeed in the stage of retrieval. Her semantic and phonological errors in naming, as well as her long hesitations and "don't know" responses are consistent with a deficit in the phonological output lexicon, and so is her difficulty in irregular plural formation. A deficit in this lexicon probably also underlies her inability to read via the sublexical route, yielding surface dyslexia (Gvion & Friedmann, 2016), as reported above in the reading section. Beyond the clear lexical retrieval deficit, Adi also showed a marked difficulty in learning new words – she could learn fewer words than her sister during the meeting, and her learning pace was much slower. This may entail that Adi also has difficulty with filling her lexicons with new material, in addition to her difficulty with retrieval of existing material. Her confusion between items from two different semantic groups – flowers and dog breeds, which were taught separately, may entail that she also has difficulty in coding new words according to their semantic features. These results may indicate that a thiamine deficiency in infancy causes not only lexical retrieval difficulty but also a difficulty in encoding novel lexical entries.

3.6. Longitudinal analysis: Adi when she was 6 years old

Adi's syntactic, lexical, and conceptual abilities were tested (by Iris Fattal and Naama Friedmann) also when she was much younger, at the age of 6;9. The comparison of her performance then and now might shed some further light as to what changes and which abilities remain impaired.

At age 6;9 Adi had impaired syntactic abilities. In a relative clause comprehension task she was able to comprehend only 2/20 sentence with object relative clauses, much lower than the control group of children of the same age ($M = 15.2$, $SD = 2.9$). She performed much better in the same comprehension task on simple sentences (19/20; $M = 19.91$, $SD = 0.3$) and on subject relatives (17/20; $M = 19.91$, $SD = 0.3$). In the subject and object relative clause production task (Adif, the same one we report above) she did not manage to produce any target relative clause and gave up, and in the sentence repetition task (the same as we report above) she refused to repeat any sentence and the task was therefore stopped. This indicates that Adi had a syntactic impairment in crossing wh-movement similar to the one we found at age 17.

Adi also showed impaired lexical abilities at age 6;9. She was asked to name 52 pictures (from the Tavor test for Hebrew vocabulary, Tavor, 2008), in which she could only name correctly 6 of the 52 pictures (whereas the age-matched control participants name correctly 38.6, $SD = 6.8$). Her errors included semantic, phonological, and morphological errors, as well as use of general verbs instead of specific target verbs (cooking → making food), or names of specific exemplars instead of category names (vehicles → car). In the Hebrew version of the ITPA subtest of auditory association (Kirk, McCarthy, & Kirk, 1968, adapted to Hebrew by Fischer, 1982), which requires sentence completion with a single word, her z-score was −6.07 compared to typically developing children of the same age. In contrast, her conceptual abilities, measured by a picture association task (Biran & Friedmann, 2007), were intact and within the norm, with 97% correct performance.

Thus, her syntactic and lexical impairments, which were detected when she was 6;9, persisted into adulthood.

4. Discussion

We examined the effect of thiamine deficiency in infancy on language in a young adult, Adi. A unique turn of events allowed us to compare her performance to a minimally different control: her twin sister. Whereas Adi consumed a thiamine-deficient baby formula for 5 months when she was one year old, her twin sister was fed with a different formula of the same manufacturer that did include thiamine. The comprehensive language assessment of the twins tested various language abilities, and showed that Adi, who had consumed the thiamine-deficient formula, has severe difficulties in sentences with syntactic movement, in inflectional and derivational morphology, surface dyslexia that led to sublexical reading aloud, voicing errors in reading aloud and in repetition of nonwords, difficulties in lexical retrieval and lexical learning, and deficits in pWM in both input and output phonological buffers. In contrast, her twin sister, Hadas, performed within the norm in all these domains. These striking differences in the language, reading, and memory abilities of the twins, who were raised in a similar environment, and were exposed to very similar language input – support the hypothesis that the cause of the language impairment shown by Adi is indeed thiamine deficiency during infancy.

Our findings also show for the first time that a young adult who had thiamine deficiency in infancy still shows language impairment in adulthood, which suggests that the language impairments caused by thiamine deficiency in infancy remain in the long term. The deficit selectively affected language, as Adi's conceptual abilities were found to be similar to her age-matched controls.

4.1. *Syntactic impairment*

Adi's difficulty with syntax was manifested in the production, comprehension, and repetition of sentences with crossing syntactic movement (such as object relatives and object questions). This syntactic impairment was present when she was tested at age 6;9, and remained through adolescence. Fattal et al. (2011) previously reported that the same difficulty was present for 97% of the five year-old children they tested and who had consumed the same thiamine-deficient formula. The syntactic deficit was selective, and Adi produced and understood simple sentences and sentences without crossing movement much better than sentences with crossing movement. This selective impairment in syntax is very similar to the impairment of children and adults with a developmental impairment in syntax termed syntactic SLI (SySLI; Friedmann & Novogrodsky, 2004, 2007, 2011; Friedmann et al., 2015; sometimes termed "syntactic DLD"), and of deaf children who were not exposed to sufficient language input during the first year of life (Friedmann & Szterman, 2006, 2011; Haddad-Hanna & Friedmann, 2009).

4.2. *Lexical retrieval and word learning*

Adi also showed lexical impairments, which were clearly evinced in her poor performance in the picture naming task. Our further analyses indicated that this lexical difficulty stemmed both from a deficit in retrieving lexical entries that are stored in her phonological lexicon and from a deficit in learning and encoding new lexical items. Her pattern of errors in picture naming, as well as the results of the priming task, indicated that at least part of her lexical failures are due to inability to correctly retrieve entries that are stored in her phonological lexicon: first, the fact that she produced erroneous responses that were phonologically or morphologically related to the target words supports the idea that the word is stored in her lexicon, possibly represented in an unstable or incomplete way. Additionally, phonological cues of first phoneme or first syllable aided her retrieval in some of the items she had failed to retrieve, again suggesting a difficulty in retrieving an existing representation. The results of the priming task also support this conclusion. The priming task was constructed with target words she had previously been unable to retrieve. Both phonological and semantic priming helped Adi in retrieving the correct word, but she was not able to retrieve words without related primes. The fact that phonological and semantic priming helped Adi with retrieval suggests that the relevant representations do exist in her lexicons, but she has difficulty accessing them, and that activating related semantic and phonological entries helps her with accessing the relevant entry. This conclusion should be taken cautiously, however, due to the small number of items in the priming task.

The plural production task, which required her to produce the regular and irregular plural form of singular nouns, indicated that her impairment in the phonological output lexicon also affects idiosyncratic information about lexical entries such as their irregular plurals.

The word-learning task showed that Adi also has a marked difficulty learning new, previously unknown words, and that her learning curve was much flatter than her sister's, meaning that her learning pace was much slower. She failed to learn most of the words while her twin mastered all words, and she produced some of the other words with phonological and/or semantic errors, as well as cross-semantic category errors, indicating that some of the words were only partially acquired. It thus seems that Adi has difficulty in encoding new items in the lexicon as well as in retrieving them, and that her poor performance in lexical retrieval and word-learning tasks is a result of the combination of both impairments.

Difficulty with lexical retrieval was found for most of the children in the thiamine-deficient group when they were 6–7 years old, as reported in in Fattal et al. (2011) study, but this deficit seemed to improve for some of the children at a later age (Fattal, 2014 for ages 8–9; Katz et al., 2019 for ages 16-17). However, Adi's lexical difficulties were evinced when she was 6;9 years-old, persisted through adulthood.

The inclusion criteria for participation in the language assessment in the previous studies required that the children started consuming the deficient formula before the age of 13 months, and consumed it as their only food source for at least one month. However, most of the children reported in Fattal et al. (2011) and in Fattal (2014) were much younger than 13 months when they started consuming the formula (for the 57 children about whom we had information – the average age of first consumption was 4.5 months, SD = 3.1, and the average age at the end of consumption was 8.1 months, SD = 3.7). Adi, in contrast, was 1;0 when the thiamine was removed from the formula she consumed, and she continued consuming the deficient formula until the deficiency was discovered, when she was 1;5. The difference in age of consumption between Adi and the other children tested previously may therefore explain why her lexical impairment has a slightly different, broader pattern.

4.3. Phonological working memory and morphology

Adi was also found to have impaired phonological working-memory, which was also reported for some of the children in Fattal (2014), using only one task of single nonword repetition. In the current study, we also assessed Adi's serial recall spans, and they were found to be below her age-norm for basic, nonword, and long-word spans, and for matching input span. She also had difficulty repeating nonwords, demonstrating a length effect, which is characteristic of low phonological working-memory. These results show that her phonological input buffer is impaired, as indicated by her limited matching span, which involves only input,[5] and can also explain her difficulty with learning new words (Baddeley, Gathercole, & Papagno, 1998; Papagno & Vallar, 1992; Shallice & Papagno, 2019). We suggest that her phonological output buffer is also impaired, and this underlies her imapired word and nonword repetition as well as her pattern of errors in reading nonwords.

Adi also showed difficulty with derivational and inflectional morphology in reading and in sentence completion tasks, a deficit that has not been previously reported for individuals who experienced thiamine deficiency in infancy. An impairment in the phonological output buffer causes morphological errors (Dotan & Friedmann, 2015; Friedmann, Stark, Gvion, & Coltheart, 2021), so they may have resulted from her phonological output buffer deficit, and her inflectional errors may also result from her syntactic deficit.

4.4. Reading

Adi's reading was also impaired: she has surface dyslexia in reading aloud, and she made voicing errors and lexicalizations in nonwords. Spektor (2012) found various types of dyslexias in the thiamine deficiency group when they were 8–9 year-old. In Adi's case, we showed that her errors can be explained by an impairment in components which are not specific to reading. Her surface errors are explained by her impairment to the phonological output lexicon, as her orthographic input lexicon is intact according to her good performance in lexical decision of pseudohomophones and her comprehension of homophones and potentiophones. Her voicing errors, lexicalizations in nonword reading, and morphological errors in reading aloud can be explained by an impairment to the phonological output buffer (or as deficits in the sublexical reading route, see footnote 4).

4.5. The bright side: intact silent reading and processing of sentences without crossing movement

Despite her widespread language impairments, Adi's performance in the reading and syntactic tasks also suggest that some of her language components are intact. In marked contrast to her many errors in reading aloud, Adi had a perfect performance in tasks that require silent reading (lexical decision and homophone association tasks). Additionally, all of her letter transpositions in the reading aloud tasks were lexicalizations of nonwords, she did not have any similar errors in existing words. This indicates that her orthographic visual analyzer – which is responsible for letter identification, position encoding, and binding of letters to words – is intact. Her orthographic input lexicon, its connection to the semantic lexicon, and the semantic lexicon itself are also intact, allowing her to identify and understand existing written words.

In addition, Adi was able to produce simple sentences and subject relatives. This suggests that her syntactic impairment is selective to crossing movement (and possibly also to agreement and tense), whereas other syntactic abilities (such as embedding and non-crossing movement) are intact.

4.6. Thiamine deficiency and critical periods for language acquisition

To sum up the findings of the language assessment, Adi's syntactic impairment is in line with previous finding about the effects of thiamine deficiency in infancy. Her lexical impairment is also characteristic, however it seems that it may be broader than in other individuals who consumed the formula, if it indeed also affects word-learning. Furthermore, it seems that at least some of the children who had impaired lexical retrieval at age 5 greatly improved at age 7–9 or 16–17, to the point where they were not significantly impaired compared to their peers. This is not the case for Adi, who was significantly impaired in lexical retrieval.

[5] We also considered the possibility that Adi does not have an impaired phonological output buffer, but only an impaired phonological input buffer, since all of the tests for phonological working-memory, besides the matching span test (which clearly showed she does have an impaired input buffer) require both input and output capabilities. Under this hypothesis, Adi's errors in tense morphology are due to her syntactic deficit, her errors in derivational morphology are due to her deficit in the phonological output lexicon, and an additional deficit in the grapheme-to-phoneme converter must be assumed in order to explain her voicing errors in reading and transpositions in nonword reading (since all transpositions were lexicalization errors, i.e., they resulted in existing words, it could be argued that they are caused by reading nonwords through the lexical route, since the sub-lexical route is impaired). However, this option has several shortcomings: This hypothesis explains similar errors by different means: voicing errors are explained by a deficit in the phonological output lexicon in naming and in reading of existing words, by a deficit in grapheme to phoneme conversion in nonword reading (and possibly in existing word reading too), and by a deficit in the phonological input buffer for nonword repetition. In contrast, a deficit in the phonological output buffer can explain all voicing errors.

The findings strengthen previous research that found that thiamine deficiency in infancy leads to impaired language and reading at a later age. We show, for the first time, that the impairment is present even in a young adult, at an age when language is normally fully developed. The fact that Adi could not "catch up" and did not develop normal language abilities regardless of many years of continuous input, whereas her twin, who was raised in a similar environment and was exposed to a very similar language input developed typical language abilities point to the reason for language impairments in the ones who received thiamine-deficient nutrition in infancy: it is the age of consumption that matters, rather than the age of testing. This finding also suggests that critical periods for development are involved: like the other infants fed by the thiamine-deficient 'Remedia' formula, Adi had consumed the formula during the critical period for first language acquisition.

Language acquisition requires the combination of innate mechanisms designated for language, and of sufficient language input (Chomsky, 1965, 1986). Natural language input is necessary to trigger the opening of the critical period, and then sufficient input must be received within a short period of time in order to enable a proper acquisition of language before the critical period closes (Lenneberg, 1967; Pallier, 2013; Penfield & Roberts, 1959; Werker & Hensch, 2015). Within the area of language, different language abilities are acquired in different critical periods (Meisel, 2013; Ruben, 1997).

Children who are not exposed to sufficient language input during the first years of life, e.g., due to deafness or in cases of social isolation, cannot develop proper language abilities even if later in life they are exposed to language input (Friedmann & Rusou, 2015; Friedmann & Szterman, 2006; Fromkin, Krashen, Curtiss, Rigler, & Rigler, 1974; Grimshaw, Adelstein, Bryden, & MacKinnon, 1998; Mayberry, 1993, 1998; Mayberry & Eichen, 1991; Mayberry & Fischer, 1989; Werker & Tees, 2005). It was shown that sufficient language input in the first year of life is crucial for the development of syntax, and especially for comprehension and production of structures involving crossing movement, such as object relative clauses, object questions, topicalization and passive constructions (Friedmann & Szterman, 2006; Szterman & Friedmann, 2003).

In the case of thiamine deficiency during infancy, the problem is not insufficient language input, but rather interference with the neural mechanisms required for language acquisition. The role of thiamine in different brain processes, especially in the developing brain, suggests that thiamine-deficient nutrition before the brain has been fully developed and during the critical period for language acquisition may interfere with language acquisition – either by blocking the opening of the critical period, or by affecting the necessary brain processes that occur within this period. Thus, children with thiamine deficiency early in life and children who are exposed to alcohol prenatally, may be susceptible to language impairments that persist later in life (Fattal et al., 2011).

Thiamine deficiency per se, therefore, does not affect language abilities. It is only when thiamine deficiency coincides with the critical period for language acquisition that it leads to language impairments. This point explains the marked difference between adults with Korsakoff's syndrome, who suffer various cognitive effects due to thiamine deficiency but do not show language impairments, and adults like the participant in the current study, who has been exposed to thiamine deficiency in infancy.

If Adi does indeed have a broader impairment as compared to other children who consumed the thiamine deficient formula, it can be explained by her relatively late age of consumption of the formula: since she consumed the formula at a later age (1;0–1;5) than the children tested previously, but still during the time known to be crucial for language acquisition, she missed more critical periods, "deadlines", for the acquisition of linguistic abilities. The exact ordering of different critical periods requires more research. However, the fact that other studies Katz et al. (2019) and Fattal (2014) showed that at least for some children the syntactic impairment remained whereas the lexical impairment improved at a later age, and that Adi had a broad lexical impairment, may suggest that the critical period for the acquisition of lexical abilities is later than that of syntax (which is known to be around 12 months, Friedmann & Rusou, 2015; Friedmann & Szterman, 2006, 2011).

5. Conclusion

We showed that thiamine deficiency during infancy, and specifically during the critical period for language acquisition, around age 1 year, caused a long-lasting language, reading, and memory impairment in a young adult, Adi. We were able to show that Adi's impairment (and by generalization, the impairments of many other individuals who consumed a thiamine deficient diet during infancy) was caused by biological factors, and not by insufficient or poor linguistic input in her environment: it is very unlikely that twins, who grew up in the same house, with the same parents and siblings, and generally spent a lot of time together, received input that is different in any essential way, to the extent that only one of them has language impairments because of it. Further research is needed in order to describe the effects of thiamine on adults' language on the group level. This recently became possible for the first time, when other individuals who had consumed the very same deficient formula as infants became adults. Furthermore, our hypothesis that the age of deficiency affects the nature of the impairment should be further tested with more data, by comparing individuals who had a deficiency at different ages during infancy, and by directly comparing the language abilities of adults who had thiamine deficiency during infancy and adults with korsakoff's syndrom.

We hope that Adi's story, as well as the untold stories of many other children who consumed the thiamine deficient formula, which demonstrates the importance of sufficient thiamine consumption during the critical period for language acquisition, will assure that such critical nutrients will never be omitted again from any baby formula, and help these individuals receive the correct treatment for their impairments.

Author contributions

YZK, NH, and NF worked together on the conceptualization, methodology, testing, error and performance analysis and statistical analysis, visualization, and all stages of writing. Supervision, resources and funding acquisition –NF.

Funding

This research was funded by Human Frontier collaboration on analog computations underlying language mechanisms (HFSP RGP0057/2016), by the Lieselotte Adler Laboratory for Research on Child Development, and by a grant from the Cukier-Goldstein-Goren Center for Mind and Language (Siloni & Friedmann, 2019).

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Tel Aviv University (protocol code 0002486-1).

Informed consent statement

Informed consent was obtained from all subjects involved in the study. The mother of the twins, as well as the twins themselves gave their informed consent for inclusion before they participated in the study.

Data availability statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical reasons.

CRediT authorship contribution statement

Yuval Z. Katz: Conceptualization, methodology, testing, error and performance analysis and statistical analysis, visualization, and all stages of writing. **Neta Haluts:** Conceptualization, methodology, testing, error and performance analysis and statistical analysis, visualization, and all stages of writing. **Naama Friedmann:** Conceptualization, methodology, testing, error and performance analysis and statistical analysis, visualization, and all stages of writing. Supervision, resources, and funding acquisition.

Declaration of competing interest

None.

Acknowledgments

We thank Adi and Hadas for their participation. We are grateful to Iris Fattal and Aviva Fattal-Valevski for their help.

Appendix A. Control Groups

Table A
Information about the control groups.

	Task	N	Tested in (if empty – unpublished results collected by lab members)	Age
Syntax	Relative clause comprehention and paraphrasing (*Meguvana*)	13	Rouso (2017)	29–69
	Relative clause production (*Adif*)			
	Sentence repetition (*PETEL*)			
Morphology	Sentence completion with morphologically-complex verbs (*HIFIL*)	21	Katz and Friedmann (2020)	20–29
Reading	*Tiltan* – Single word reading	944		18+
	Tiltan – nonwords reading	883		18+
	Tiltan – word pair reading	978		18+
	Tiltan – Potentiophones	372		18+
	Tiltan – migratable words	452		18+
	Migratable word pairs (*Kishbion*)	443		18+
	Morphologically complex nonwords (*Cilkiyot*)	40	Stark (2020), Friedmann et al. (2018)	20+
	Homophone association	141	Gvion and Friedmann (2016)	20+
	Written pseudohomophone lexical decision	148		
pWM	Serial recall (*FriGvi*)	136 (basic), 19 (long), 148 (nonword)	Gvion and Friedmann (2012a)	20–30
	Matching span (*FriGvi*)	10		
	Nonword repetition (*BLIP*)	20	Khentov-Kraus and Friedmann (2018)	23–48

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