EFFECTS OF BIRTH EXPERIENCE ON RELATIONAL MEMORY IN ADULTS

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Abstract

Recent evidence has emerged that being born via planned or emergency cesarean section delivery (CSD) compared to vaginal delivery (VD) not only led to slower allocation of attention in human infants and adults but also affected hippocampal regions responsible for memory in mice. This is concerning as the number of C-sections has risen in the past two decades according to the World Health Organization. Therefore, the current study investigated if a higher-order cognitive function like relational memory is also affected by CSD and if these effects last into adulthood. Birth experience effects on item-item, itemspace and item-time relational memory along with item recognition were assessed in adult participants using a task developed by Konkel et al. (2008). Results indicated that the itemitem memory performance was affected by CSD with planned CSD adults showing poorer recognition compared to emergency CSD adults. No differences in memory performance were found between either of the CSD groups and the VD group in any of the relational conditions. As relational binding has implications in forming autobiographical memories and connections between our past, present and future states, healthcare professionals should discuss with expecting mothers the potential long-term effects of planned CSD on their infants' cognitive development.

Keywords: relational memory, binding, birth experience, cesarean section, item-item memory

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Effects of Birth Experience on Relational Memory in Adults

Memories of past experiences that took place at a specific time and place are known as episodic memories (Tulving, 1972, 1983) and are critical in guiding our present behavior and planning our future behavior (Bauer, 2006). A defining feature of episodic memory is relational memory which is binding together the elements of an experience (Olson & Newcombe, 2014). Relational binding allows us to remember a person's name along with their face, an object's or a person's location or the sequence in which various events occurred (Konkel & Cohen, 2009; Olson & Newcombe, 2014). This ability to form relational memories develops rapidly throughout early to middle childhood (Ngo et al., 2018) and reaches adult-like levels only by late childhood, around 9 to 11 years of age (Barr & Rovee-Collier, 2012; Lee et al., 2015). The developmental trajectory of relational memory, however, may be influenced by certain events experienced early in life, as early as at the time of birth.

Certain birth-related events have been found to affect memory in infancy and later in life. Gestational diabetes, for example, negatively affected performance in item-time memory tasks requiring recall of a sequence of actions in infants (DeBoer et al., 2005) and pre-school aged children (Riggins et al., 2009). Another factor that affected associative memory in infants (Heathcock et al., 2004) and in adults (Kalpakidou et al., 2012) was pre-term birth. Pre-term born adults also had slower reactive latencies and used compensatory brain mechanisms to cope with the increasing cognitive workload in a working memory task (Daamen, 2015). In addition, experiencing hypoxic-ischemic injuries at birth affected infants' ability to recognize scene-face pairs compared to typically developing infants (Wagner et al., 2020). Animal models, too, provide evidence of the long-term effects of birth-related events on memory where adult rats had working memory impairments in a Morris maze when exposed to hypoxic-ischemic injuries at birth (Arteni et al., 2003) and showed deficits in spatial learning and memory retrieval when exposed to prenatal stress (Modir et al.,

2014). Overall, the events surrounding the birth of an individual have the potential to affect the ability to form associations between event details in the long-term.

Recent studies have found that another birth-related event called the mode of delivery, that is, being born via Caesarean Section Delivery (CSD) or Vaginal Delivery (VD), has differential effects on attentional mechanisms that persist into adulthood (Adler & Wong-Kee-You, 2015; Rahimi & Adler, 2019; Stevens, Adler, et al., under review). For example, visuospatial attention was slowed in both infants (Adler & Wong-Kee-You, 2015) and adults (Stevens, Adler, et al., under review) born via CSD compared to those born via VD in a spatial cueing task. Furthermore, infants delivered via planned CSD exhibited slower reflexive attention than those delivered via emergency CSD or VD. In adults, on the other hand, the CSD group had slower reflexive attention than the VD group regardless of being delivered via planned or emergency C-section (Rahimi & Adler, 2019). Birth experience effects were found to extend to memory as well in which Deoni et al. (2018) showed that CSD affected brain regions responsible for memory in children. Additionally, findings from animal models have shown that multiple brain regions are affected by CSD in mice pups including hippocampal regions (Castillo-Ruiz et al., 2018; Cheisa et al., 2018; Huang et al., 2019; Morais et al., 2020).

Such birth experience effects on hippocampal regions could consequently affect their respective functions, that is, forming and retrieving relational memories (Olson & Newcombe, 2014). The differences found in attentional allocation due to the type of CSD especially necessitate probing into how memory, a closely related cognitive function (Chun & Turk-Brown, 2007; Craik & Lockhart, 1972; Lockhart & Craik, 1990; Wolfe, 2021), may be affected by being born via CSD on a pre-determined delivery date set by the doctor (planned CSD), compared to being born via CSD after the mother has experienced initial stages of labor (emergency CSD). More importantly, the effects of birth experience on

relational memory have not yet been studied in human participants or if they last into adulthood. The current study, therefore, sought to address this gap by investigating the potential effects of birth experience (CSD or VD) on relational memory in adult participants, and whether being born via planned or emergency CSD had differential effects on relational memory performance.

Relational Memory Formation and Hippocampal Development

Relational memories are formed when individual elements of an event are tied together to make a network of representations (Konkel & Cohen, 2009). This ability to bind event information has been traced to brain regions involving medial temporal lobe (MTL) structures and the hippocampus (Olson & Newcombe, 2014). The MTL and hippocampus are critical in forming item-item relations (i.e., between features of an event) (Kohler et al., 2005), item-time relations (i.e., when an event occurred) (Ekstrom & Bookheimer, 2007), and item-space relations (i.e., where an event occurred) (Pathman & Ghetti, 2016). Research involving hippocampal lesions has confirmed that any damage to the hippocampus could result in relational memory deficits. A neuroimaging study, for instance, showed that adult amnesiac patients with MTL lesions had significant impairment in a relational memory task for object-location associations over a short delay of 8 seconds (Olson et al., 2006). Hannula et al. (2007) found using eye-tracking that amnesiac patients with hippocampal damage had poor spatial recognition memory and did not show preferential viewing towards the correctly matched face-scene pairs. Konkel et al. (2008) also demonstrated in their study that adults with hippocampal lesions were equally impaired in their ability to form all three relations, that is, item-item, item-space and item-time, thus highlighting the role of the hippocampus in all three types of relational memory.

Further division of hippocampal regions associated with basic episodic and spatial memory processes include the dentate gyrus, Cornu ammonis or CA1, CA2, and CA3

subfields (Bachevalier & Vargha-Khadem, 2005). Of these regions, the CA1 and CA2 subfields mature early but the development of the CA3 subfield and the dentate gyrus is protracted compared to the rest of the hippocampus (Bachevalier & Vargha-Khadem, 2005; Lavanex & Lavanex, 2013). The maturational changes in the hippocampus slow down two years after birth but continue up to 11 or 12 years of age (Ghetti et al., 2010; Lee et al., 2015; Riggins et al., 2018). Small additional increases in hippocampal volume, however, occur throughout adolescence and early adulthood (Bachevalier & Vargha-Khadem, 2005). Given that relational memory requires the hippocampus which is slow to develop, it is not surprising that the ability to form relational memories develops slowly as well (Olson & Newcombe, 2014; Pathman & Ghetti, 2016).

Parallel to these neural changes, there are age-related improvements in the ability to form relational memories (Lee et al., 2015; Riggins et al., 2018). Within the development of relational memory, there are different trajectories for different types of relational memory. Item-item, item-space and item-time relations develop from early to late childhood (Friedman & Lyon, 2005; Riggins, 2014; Shing et al., 2008), each reaching adult levels at different stages. Specifically, memory for spatial relations reaches adult levels by approximately 9.5 years, memory for temporal relations by 11 years and memory for item-item relations continues to develop into adolescence (Guillery-Girard et al., 2013; Konkel et al., 2008; Lee et al., 2015). When comparing the types of relational binding in children and adults, studies showed that participants performed better in the item-space or item-time binding conditions compared to the item-item binding condition (Konkel et al., 2008; Lee et al., 2015), possibly due to the continued development of the ability to bind item-item relations after childhood (Lee et al., 2015).

Hippocampal development is, therefore, structurally and functionally protracted after birth (Lee, Johnson & Ghetti, 2017; Riggins et al., 2018). As the hippocampus continues

developing into childhood, it is vulnerable to being impacted by early experiences.

Consequently, exposure to the different types of birth experience may set individuals on divergent developmental trajectories in terms of relational memory. As will be discussed in detail later, if the neural substrate for relational memory is affected at the time of birth due to birth experience, the ability to bind event details could be impacted as development progresses, leading to differential memory performance during childhood or adulthood.

C-section Births and Cognitive Development

Birth experience effects on general health and cognitive development have only recently been identified. There is growing evidence of the potential negative consequences of CSD in the form of increased risk of contracting diabetes (Cardwell et al., 2008), becoming obese (Flemming et al., 2013), developing asthma and celiac disease (Tribe et al., 2018) and has been associated with neurodevelopmental disorders such as autism and attention deficit disorder (Curran et al., 2015; Polidano et al., 2017). This is concerning as the World Health Organization (2021) reported that the number of CSD births has risen globally from around 7% in 1990 to 21% present day, and accounts for every 1 in 5 of all childbirths. This number is predicted to rise to almost 29% or one-third of all births by 2030. Consequently, there is an urgent need to assess the relative effects of CSD and VD on neural and cognitive development. The latest findings that CSD births have long-term implications on attentional development only re-enforce this claim (Rahimi & Adler, 2019; Stevens, Adler et al., under review).

CSD effects on attention were initially found in infants using eye-tracking, where 3-month-olds performed either a Posner (1980) spatial cueing task or a visual expectation task (Adler & Wong-Kee-You, 2015). The spatial cueing task, thought to be driven by bottom-up attentional mechanisms (Theeuwes & Belopolsky, 2010), was used to measure reactive latencies, or eye movements exhibited towards the target location reflexively or in reaction to

the onset of the target stimulus (Adler & Haith, 2003). The visual expectation paradigm, on the other hand, thought to activate top-down attentional mechanisms, was used to assess voluntary anticipatory eye movements guided by cognitive expectations of where the target would appear before the onset of the target stimulus (Adler & Haith, 2003; Adler et al., 2008; Haith et al., 1988). Infants' reactive latencies were found to be significantly slower in the CSD group in the spatial cueing task (Adler & Wong-Kee-You, 2015). The results with the visual expectation task did not show any differences in the proportion of anticipations made by VD infants and CSD infants but their reactive latencies did differ in a manner like that of the spatial cueing task. When the same spatial cueing task was administered to CSD and VD adult participants, CSD adults were found to initiate saccadic eye movements significantly slower than VD adults (Stevens, Adler et al., under review). The findings from these studies led the researchers to conclude that birth experience influences stimulus-driven, reflexive attention (bottom-up) but cognitively driven, voluntary attention (top-down) is relatively unaffected (Adler & Wong-Kee-You, 2015; Stevens, Adler et al., under review).

A subsequent study further investigated the differential effects of birth experience on bottom-up versus top-down attentional mechanisms in infants and adults using a visual search task (Rahimi & Adler, 2019). Search asymmetry was assessed using eye-tracking since visual search involving feature-present targets produces strong bottom-up saliency signals whereas search involving feature-absent targets produces weak bottom-up saliency signals (Adler & Gallego, 2014; Wolfe, 1994). Results indicated that the stimulus-driven reactive latencies were slower in CSD infants and adults compared to VD infants and adults. Furthermore, the CSD groups were divided into planned and emergency CSD sub-groups based on potential theories regarding different mechanisms by which CSD might affect visual attention (Cryan & Dinan, 2012; Galland, 2014; Toda et al., 2013). The planned CSD infants had slower stimulus-driven reflexive attention compared to emergency CSD and VD infants but there

were no differences between emergency CSD and VD infants (Rahimi & Adler, 2019). In adults, both planned and emergency CSD groups had slower stimulus-driven reflexive attention than the VD group. Birth experience, however, was not found to affect cognitively driven, top-down attention. CSD, therefore, affected bottom-up attention in both infants and adults suggesting that the development of attentional mechanisms could be permanently impacted (Rahimi & Adler, 2019). Moreover, the emergency CSD infants performed similarly to VD infants and were significantly faster than planned CSD infants, but the results with adult participants indicated that the difference between emergency and planned CSD groups disappeared in adulthood and both CSD types became slower at allocating visual attention.

The above findings with birth experience differences in the operation of attentional mechanisms could have implications for memory processes since attention and memory cannot operate without each other (Chun & Turk-Browne, 2007). Attention is essential during encoding and for subsequent accurate retrieval of memory (Chun & Turk-Browne, 2007; Craik & Lockhart, 1972; Lockhart & Craik, 1990; Wolfe, 2021). Generally, relational information compared to item information requires more attentional resources and intentional processing to encode and to retrieve (Troyer & Craik, 2000). The important role of attention in forming memories has been formalized in models such as the Levels-of-Processing Theory (LOP) (Craik & Lockhart, 1972) and the Guided Search Model (Wolfe, 1994; Wolfe, 2021). In the LOP, the cognitive system is suggested to be structured hierarchically where shallow levels of analysis are concerned with sensory and physical stimuli while deeper levels of analysis are concerned with abstract, semantic, and associative processes (Craik & Lockhart, 1972), and that deeper analyses, in general, require more attentional resources (Lockhart & Craik, 1990). A memory trace acts as a record of these analyses and becomes more durable with increasing depth of processing or elaborative processing such that retrieval of the event

details becomes easier. Therefore, the allocation of adequate attentional resources could lead to deeper encoding and stronger and more enduring traces for retrieval (Craik & Lockhart, 1972; Lockhart & Craik, 1990).

In the Guided Search Model (Wolfe, 1994; Wolfe, 2021), a series of processes have been proposed to occur for object recognition starting with directing selective visual attention to the items or different features that make up the item. Selective attention toward the items or their features would be guided based on an attentional "priority map" created by contributions from multiple sources of guidance including parallel processes of bottom-up and top-down attention. Bottom-up activation guides attention toward distinctive items in the visual field and is automatic whereas top-down, user-driven activation guides attention to the desired item and if the features of an item are not unique (Wolfe, 1994). The priority map changes with changes in the visual field as attention is deployed from one spatial location to another. The selected object of attention is then represented in working memory, the contents of which prime subsequent deployment of attention using a top-down "guiding template."

Another "target template" held in activated long-term memory can be matched with the current object of attention in working memory to determine if that object is a target item and, if it is, the search for the target object terminates and object recognition is deemed successful (Wolfe, 2021).

The differences found in visual attention between CSD and VD adults (Stevens, Adler et al. (under review); Rahimi & Adler, 2019) then brings into question how attentional resources would be adequately used when episodic details such as item-item, item-space, or item-time relations are required to be encoded within a few seconds as tested in previous relational memory studies (e.g. Hannula et al., 2007; Konkel et al., 2008; Lee et al., 2015; Riggins et al., 2014). Since CSD adults, both planned and emergency, are slower to allocate visual attention compared to VD adults (Rahimi & Adler, 2019; Stevens, Adler et al., under

review), they may not be able to selectively allocate attentional resources required to encode the different features of the stimuli (Wolfe, 2021) within a limited encoding time for binding to occur. Consequently, CSD adults could exhibit inaccurate recognition of event details as the relational information may not be processed sufficiently deeply or elaborately to be distinctively encoded in the first place (Craik & Simon, 1980; Lockhart & Craik, 1990; Jacoby & Craik, 1979).

Potential Negative Consequences of C-section on Relational Memory Formation

Apart from the findings regarding CSD effects on visual attention, studies with human infants and animal models have provided evidence for the effects of CSD on brain regions responsible for relational memory formation. For example, Deoni et al. (2018) found that two-week-old VD neonates had better neural connectivity in white matter regions in the frontal, parietal, and temporal lobes than CSD neonates. In animal models, CSD was found to influence neurochemical responses that occur in mice due to the stress of birth such as decreased UCP2 (Uncoupling Protein 2) expression in the hippocampus which is a protein shown to promote neuronal differentiation, axonal outgrowth and synapse formation in the hippocampus (Seli & Horvath., 2013) and is associated with learning and memory (Wang et al., 2014).

CSD was also found to influence neuronal cell death in mice pups (Castillo-Ruiz et al., 2018). Neuronal cell death is a common developmental process that occurs in all mammals in the perinatal period, where approximately 50% of the neurons initially generated are eliminated (Castillo-Ruiz et al., 2020). Along with neuronal cell death, the stress of birth induces neuro-endocrinal responses such as the release of vasopressin and this was found following a VD birth in humans and rats but not in planned CSD births (Chard et al., 1971; Wellman & Bührer, 2012). In line with this, Castillo-Ruiz and colleagues (2018) found that CSD mice pups had unchanged or increased cell death in many brain regions whereas VD

mice pups had an abrupt decrease in cell death and suggested that VD is neuroprotective due to the release of vasopressin. The sites of increased neuronal cell death in CSD pups included the dentate gyrus, the CA1 subfield, principal bed nuclei of the stria terminalis, lateral habenula and dorsal raphe. CSD mice pups also had shorter CA3 pyramidal neurons in the hippocampus due to delayed dendritic arborisation (i.e., branching out of dendrites which helps in making new synaptic connections) (Chiesa et al., 2018). As reviewed by Olsen et al. (2012), the CA1 and CA3 subfields of the hippocampus are involved in the transmission of information necessary to perform relational binding. In addition to binding, they are also involved in a comparison process where the newly formed relational representations may be compared to the current perceptual input or to previously stored representations. These regions being affected due to CSD may in fact affect their functional role in the formation of relational memories.

The effects of CSD on rat pups can be compared with previous animal studies in which extensive bilateral neonatal hippocampal lesions prevented object recognition and relational learning (Bachevalier et al., 1999), delayed the emergence of memory for spatial locations, and completely eliminated memory for object-place associations in adult rhesus macaque monkeys (Blue et al., 2013). Though any such hippocampal injury in CSD infants may not be as extensive as that experienced by the infant monkeys in the animal studies, relational memory can still be affected even with minor hippocampal insult (Isaacs et al., 2003) due to inadequate myelination, thus, disrupting hippocampal maturation (Bachevalier & Vargha-Khadem, 2005; Lavanex & Lavanex, 2013). An interesting suggestion by Bachevalier and Vargha-Khadem (2005) to be noted is that the effects of perinatal hippocampal insult resulting in memory impairment may not be evident at an early age but gradually emerge in the middle childhood years. Furthermore, by providing the example of children with developmental amnesia, they suspected that the precursors for hippocampal-

dependent memory may be present shortly after birth but may fail to mature into context-rich hippocampal-dependent functions until later in life (Bachevalier & Vargha-Khadem, 2005). What can be inferred from this is that any CSD-related effects on hippocampal-dependent memory could emerge only in adolescence or adulthood.

Another reason to believe that VD is neuroprotective apart from the labor-induced hormonal changes during birth is the 'bacterial baptism' hypothesis. Passage through the birth canal is suspected to lead to the seeding of the gut microbiome (Cryan & Dinan, 2012). VD infants, therefore, are exposed to the bacteria while passing through the vaginal canal (Bezirtzoglou, 1997) whereas CSD infants do not get this opportunity and are exposed to bacteria from the mother's skin, breastmilk and the hospital's environment (Grölund et al., 1999). Recent findings regarding the communication between gut microbiota and the central nervous system assert the importance of 'bacterial baptism' and that it may play a role in cognitive development (Cryan & Dinan, 2012; Galland, 2014). Consequently, CSD births could lead to disturbed gut microbiota composition which, in turn, could have potential negative consequences on cognitive functioning in the long term (Polidano et al., 2017).

Taken together, CSD may cause relational memory deficits in adults by affecting hippocampal cells at birth and the course of hippocampal maturation. However, there are studies that show that any CSD effects on different brain regions found at birth either minimize with age or become non-existent in adulthood. For example, Deoni et al. (2018) found that human infants born via CSD had reduced myelin in frontal, temporal, parietal, and occipital areas, all areas associated with multiple cognitive processes including memory and attention during infancy, but the myelination process normalized with age, and no changes were found in cognitive outcomes beyond three years of age. Animal models, too, provide similar conclusions where no long-term effects of CSD on hippocampal maturation were found in the adult offspring of mice (Cheisa et al., 2018; Huang et al., 2019). More recently,

Huang et al. (2019) found that planned CSD affected glucocorticoid function in the hippocampus in offspring of mice and was associated with impairment in learning and memory during adolescence but not in adulthood, indicating that CSD effects on memory may after all, be non-permanent.

Nevertheless, evidence provided from studies that did find long-term negative effects of the nature of birth (Arteni et al. 2003; Kalpakidou et al., 2012; Modir et al., 2014) and CSD (Rahimi & Adler, 2019; Stevens, Adler, et al., under review) on cognitive development encourage further study of whether birth experience effects endure into adulthood. For instance, the attentional differences found in adulthood, due to planned or emergency CSD (Rahimi & Adler, 2019; Stevens, Adler, et al., under review) might impact associated functions such as memory for event details, especially when both cognitive functions are found to similarly activate multiple brain regions, including the medial temporal lobe regions (Cabeza et al., 2003) that are responsible for relational binding (Olson & Newcombe, 2014). If these brain regions were affected by CSD during birth, CSD adults may show poorer memory accuracy compared to VD adults due to slowed visual attention and insufficient relational binding. Moreover, studies with animal models have indicated that planned CSD births do not reap the neuroprotective benefits of maternal labor that VD births do (Castillo-Ruiz et al., 2018; Huang et al., 2019; Seli & Horvath, 2013). As a result, planned CSD births may show even poorer cognitive outcomes compared to emergency CSD births since emergency CSD is performed due to some birth complications that may have occurred after the mother undergoes initial stages of labor, thus giving the neonates an opportunity to experience some neuroprotective effects of labor. Consequently, there is a need to understand if birth experience, that is, being born via planned CSD, emergency CSD or VD, differentially impacts the ability to form relational memories and if such effects manifest in adulthood.

Current Study

The goals of the current study were to (a) investigate the effects of birth experience, CSD or VD, on relational memory processes in adults, and (b) if being born via planned CSD led to poorer ability to bind event information, compared to emergency CSD or VD, in adulthood. Based on preliminary studies that found developmental differences between planned CSD, emergency CSD and VD birth experience groups on attention (Rahimi & Adler, 2019) and CSD effects found on the hippocampal regions responsible for relational memory (Castillo-Ruiz et al., 2018; Chiesa et al., 2018; Huang et al., 2019), all three types of binding processes, that is, item-item, item-space and item-time binding, are required to be assessed in adult participants. To this end, the current study used a within-participant paradigm proposed by Konkel et al. (2008) which assessed the three types of relational memory using a single encoding procedure.

Konkel et al. (2008) in their study, used a single task to compare item memory and relational memory performance between adult participants with hippocampal lesions and those with an intact hippocampus. The stimuli used in their task were novel, abstract shapes to which participants had no prior exposure to minimize the influence of pre-existing experiences that the participants may have had with them. Other studies that had applied this paradigm had taken this step to prevent age-related differences in performance in the use of semantic-based organizational strategies or unitization (Lee et al., 2015) or to minimize potential group differences in the use of verbal strategies between adults with autism spectrum disorder and typically developing adults (Ring et al., 2015). The task used in this paradigm by Konkel et al. (2008) involved blocks of encoding and retrieval phases where the novel stimuli were presented in sets of three under four different conditions. The four conditions involved an item recognition condition and three relational conditions that required binding of item-item, item-space, and item-time relations. The same task was used in

a study by Lee et al. (2015) to explore age-related differences in binding processes but with slight modifications to the task procedure. The abstract stimuli were also presented in sets of three for each trial but were referred to as 'triplets' and the task was called the Triplet Binding Task (TBT).

As found in previous studies that used the TBT, all adults were expected to show decreased performance in the item-item binding condition compared to item-space and item-time conditions as this was found to be the most challenging condition (Konkel et al., 2008; Lee et al., 2015; Ring et al., 2015). As a function of birth experience, VD adults were predicted to perform better than CSD adults in all three relational conditions considering that VD adults would be more capable of attending to and performing multiple binding operations within a limited exposure time to novel stimuli based on attentional differences found between VD and CSD groups (Rahimi & Adler, 2019; Stevens, Adler, et al., under review). Furthermore, findings from the study that assessed attention (Rahimi & Adler, 2019) with different birth experience groups, inspired the prediction that adults born via planned CSD or emergency CSD would show decreased ability in binding item-item, item-space, and item-time relations compared to adults born via VD and that planned CSD adults would perform even worse than emergency CSD.

Method

Participants

Participants were 81 full-term born adults (25 males and 56 females) recruited from the York University Undergraduate Research Participant Pool (URPP) and received course credit for their participation. The sample consisted of adults ranging between the ages of 18 and 35 years (M = 20.56, SD = 3.34) with 41 individuals belonging to the VD group and 40 individuals belonging to the CSD group. The CSD group further consisted of 16 individuals who were delivered via emergency CSD, and 24 individuals delivered via planned CSD.

Participants were recruited from a diverse population and the final sample included South Asian (n = 20), Black, African American, or African Canadian (n = 19), White or Caucasian (n = 13), Chinese (n = 5), West Asian (n = 5), Arab (n = 4), Latin American (n = 3), Filipino (n = 1), Korean (n = 1) and Mixed Race (n = 10) individuals. Family incomes reported were either less than \$20,000 (n = 8), between \$20,000 and \$40,000 (n = 14), between \$40,000 and \$60,000 (n = 13), between \$60,000 and \$90,000 (n = 16), between \$90,000 and \$120,000 (n = 12), between \$120,000 and \$150,000 (n = 7), or more than \$150,000 (n = 11).

Stimuli and Apparatus

The task was administered using online platforms such as Qualtrics (Qualtrics, Provo, Utah, 2005), Inquisit 6 (Millisecond, Seattle, Washington, 2020), and Zoom (Zoom, San Jose, California, 2011) on an ASUS VivoBook S14 laptop. The consent and demographic forms were prepared in Qualtrics, and the TBT was programmed using Millisecond Inquisit 6.

Zoom was used to administer and monitor the task online. Participants were required to download Inquisit 6 Player for completing the task on their own computers and were provided a step-by-step guide to do so during the first few minutes of the Zoom session depending on whether they used a Windows or Mac operating system.

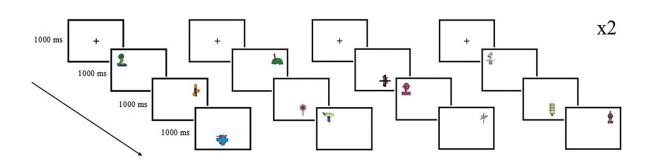


Figure 1. Examples of Some Novel Stimuli Used in the TBT

The stimuli used were 464 color images of novel objects created by Ryan and Villate (2009) using CorelDraw v.12 (Corel, Ottowa, Ontario, 2004). Each of the novel objects used was a multi-colored random combination of shapes that bore little to no resemblance to real-world objects (Figure 1). The novel objects were used as stimuli for the TBT to ensure that

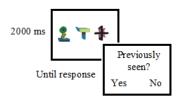
participants had no prior exposure to or pre-existing representations of them and to hamper the use of any semantic-based organizational memory strategies that could aid in forming relational memories (Konkel et al., 2008; Lee et al., 2015). Out of the 464 stimuli, 48 stimuli were randomly chosen for the practice phase and the rest were used for the actual TBT. The stimuli were presented on a white background (Figure 2) with the screen size fixed at 14-inches such that the stimuli appeared 4cm x 4cm in size regardless of the size of the laptop screen or computer monitor used by the participants.

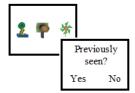
A.)



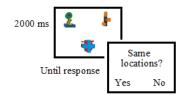
B.) Target Lure

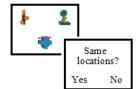
i)



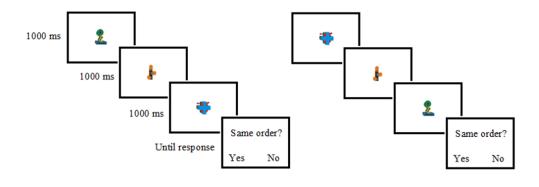


ii)





iii)



2000 ms

Same
group?
Yes No

Yes No

Figure 2. Example of an Encoding Phase and Examples of Probe Trials in the Triplet Binding Task. A) Example of an encoding phase where all four triplets were presented twice in the same order. B) Examples of target and lure probe trials for (i) item-recognition, (ii) item-space, (iii) item-time, and (iv) item-item conditions.

Task Design

The TBT was designed by Konkel et al. (2008) to assess the ability to remember itemitem, item-space, and item-time relations in addition to item recognition memory. In the current study, each of these memory types was assessed in separate blocks, resulting in four condition blocks. In each condition block, there were eight encoding-then-retrieval phases (see Appendix A). Each encoding phase consisted of four unique triplet sequences presented twice, that is, eight encoding trials, in a repeated order. Each of the encoding trials consisted of a set of three unique images (triplet) presented sequentially at three different locations on the screen (upper left, upper right, or lower center), such that all three locations were

equidistant and appeared at a visual angle of approximately 5.53° from the visual center of the 14-inch sized laptop screen (visual angle subject to change due to less control over the distance between the seated participant and the screen). The retrieval phase immediately followed each encoding phase and included four trials. Each retrieval trial presented a probe triplet to test memory accuracy. Out of the four retrieval trials, two were target trials and two were lure trials. Depending on the condition block, target trials involved presenting the probe triplets as in the encoding phase, that is, the triplets had the same images at the same locations, in the same ordinal positions, or as part of the same triplet. In contrast, lure trials involved presenting the probe trials in a fashion different from that of the encoding phase with new images, switched locations, switched ordinal positions, or replacing one of the images in a triplet with an image from another triplet viewed in the same encoding phase. In total, there were 64 encoding trials and 32 test probes (16 target and 16 lure trials) in each condition block.

Randomization was done at each step while programming the task on Inquisit 6. The 416 stimuli reserved for the TBT were randomly assigned to each of the four condition blocks and this was done for every participant. The assigned stimuli were then randomly divided into sets of three called triplets, each condition yielding 32 encoding triplets. From this pool of triplets, each encoding phase randomly chose four unique triplets to be presented sequentially. In the retrieval phase, one of the triplets shown during the encoding phase was randomly picked to be the target or lure trial and was never selected twice, meaning that all four triplets shown during the encoding phase were used as memory probes in the retrieval phase. The order of presentation of target and lure trials in each retrieval phase was also randomized.

Procedure

All participants who signed up for the study through the York University URPP provided their informed consent and completed the demographic information form prior to the Zoom session. During the Zoom session, every participant was instructed to close other applications, turn off notifications, share their screen and always keep their microphone on while performing the task. This was done so the researcher could monitor their progress and make note of any unexpected disturbances due to the study being online which gives the researcher limited control over environmental variables. A practice session task link was shared at the beginning of the zoom session during which the participant was instructed to sit at arm's length from their computer or laptop screen throughout the task after which the TBT instructions were explained using illustrations (see Appendix B). Participants were then given four practice encoding-then-retrieval phases, one for each of the four conditions, and were reinstructed, as necessary, after which the participant was redirected to the actual TBT session webpage.

The item-recognition condition block was presented first for all participants followed by the relational memory condition blocks. The order of presentation of the three relational memory blocks was counterbalanced across participants. Participants were not told which test block would appear first or next and were instructed to remember all four kinds of memory information throughout the session, that is, the images, the triplet group they belonged to, their locations and their order of presentation. As the TBT has been reported to be quite difficult by previous studies that used this task (Konkel et al, 2008; Lee et al., 2015; Ring et al., 2015), a break of three minutes was given for all participants after they completed the first two test blocks to reduce any effects of memory load or tiredness that may have been caused by the task.

TBT Encoding Phase

In each encoding phase, four unique trials were presented twice. Each trial included a triplet sequence of novel images (see Figure 2A). A fixation cross was presented at the beginning of each encoding trial for 1000 ms, which focused all participants' attention on the center of the screen prior to stimulus presentation and served as an inter-trial interval. Each of the triplet images was then individually presented for 1000 ms at one of the three locations, one immediately after the other with no inter-stimulus interval. The four encoding triplets were presented once again in the same order, giving participants one more chance to encode the images and their relational information within each triplet. The procedures for the encoding phase were identical for each of the four condition blocks.

TBT Retrieval Phase

Each encoding phase was immediately followed by the retrieval phase and tested memory for item recognition, item-item, item-space, or item-time relations depending on the condition block. In every retrieval phase, memory was tested with four probe trials including two targets and two lures. In all condition blocks, the task did not progress to the next retrieval trial until a response was given to the question displayed after the presentation of the retrieval probe.

Item recognition. In this condition, three images from an encoding sequence were simultaneously presented in a horizontal line across the center of the screen for 2000 ms, and participants had to determine whether all the images were presented during the encoding phase. At the offset of the three images, the question "Previously seen?" was displayed and participants had to select either the "Yes" or "No" buttons on the screen (see Figure 2B (i)). For the target trials, three previously studied images from the same encoding phase were presented. For the lure trials, one of the images was previously studied while the other two were new images.

Item-space binding. In this condition, three images from the encoding sequence appeared together on the screen for 2000 ms and participants had to determine whether the images were in their original locations or not. At the offset of the three images, the question "Same locations?" was displayed and participants had to select either the "Yes" or "No" buttons on the screen (see Figure 2B (ii)). For the target trials, the three images appeared in their original locations as presented in the encoding phase. For the lure trials, two of the three images had switched their respective locations.

Item-time binding. In this condition, images from the encoding sequence appeared sequentially at the center of the screen, each for 1000 ms, and participants had to determine whether the images had appeared in their original sequence or not. At the offset of the last image, the question "Same order?" was displayed and participants had to select either the "Yes" or "No" buttons on the screen (see Figure 2 B (iii)). The three images were presented in their original sequence for the target trials whereas two out of the three images had switched their ordinal positions for the lure trials.

Item-item binding. In this condition, three images from an encoding sequence were simultaneously presented in a horizontal line across the center of the screen for 2000 ms, and participants had to determine whether the images presented belonged to the same encoding triplet. At the offset of the last image, the question "Same group?" was displayed and participants had to select either the "Yes" or "No" buttons on the screen (see Figure 2 B (iv)). For the target trials, the three images appeared from the same encoding triplet and for the lure trials, one of the three images was replaced by an image from another triplet that was presented in the same encoding phase.

For all target trials, the correct response was "Yes" and for all lure trials, the correct response was "No." Participants were instructed to select "No" if they thought that even one

of the three images displayed in the probe trial was different from what they had seen during the encoding trial. Reaction times for the responses were recorded as the time taken for each participant from the time the options "Yes" or "No" were displayed until a response selection was made.

Data Reduction and Analysis

Responses were categorized as hits, false alarms, misses and correct rejections. Specifically, responses were categorized as "hits" if the participants correctly chose "Yes" for the target trials, as "correct rejections" if participants correctly chose "No" for the lure trials, as "misses" if participants incorrectly chose "No" for target trials, and as "false alarms" if they incorrectly chose "Yes" for the lure trials. If any of the participants failed to discriminate old from new images in the item-recognition condition (hits - false alarms \leq 0), that participant's data was to be excluded from further analyses; however, no such instances were found. Hit and false alarm rates were then calculated for each group. A correction of 0.5 was added to each of the response category bins, as done in the study by Konkel et al. (2008), to eliminate any instances of zero hits, false alarms, misses or correct rejections thus preventing the occurrence of infinite d' scores. To measure the overall relational memory function, each of the relational conditions' hits, misses, false alarms, and correct rejections were summed, respectively and were then used to obtain an overall d' value for each participant.

For the statistical analyses, preliminary ANOVAs were conducted to compare the relational memory performance between the CSD and VD groups and, between the planned CSD, emergency CSD, and VD groups, to check for interaction effects between the birth experience groups and the memory conditions. Planned comparisons were then run to compare the performance of the birth experience groups for each memory condition and their overall relational memory d' scores. The planned comparisons were formulated based on the

two key questions that were investigated in the current study: (a) Do CSD and VD adults differ in their item and relational memory performance in the TBT due to previous findings regarding the influence of CSD on attentional performance (Rahimi & Adler, 2019; Stevens, Adler et al (under review); Wong-Kee-You & Adler, 2015) and brain regions responsible for relational memory (Castillo-Ruiz et al., 2018; Cheisa et al., 2018; Huang et al., 2019)? and (b) Do the birth experience types, emergency CSD, planned CSD and VD differentially influence memory performance in all four conditions of the TBT as each of the birth experience types was previously found to differentially influence the allocation of visual attention (Rahimi & Adler, 2019)? To assess the first question, planned comparisons were run between the performance scores of CSD adults and VD adults for each of the memory conditions. For the second question, planned comparisons were run between (a) planned and emergency CSD groups, (b) emergency CSD and VD groups, and (c) planned CSD and VD groups for each memory condition, and with the overall relational memory score to gauge if the different birth experience types influenced the general functioning of relational memory.

In addition, reaction times were measured to make sure that participants were focused on the task since there was no time limit for response selection and unexplained extraneous factors could have influenced memory performance due to the online administration of the TBT. If the participants had unreasonably short mean reaction times (e.g., clicking responses immediately without processing the question on the screen), or long mean reaction times (e.g., inactivity for more than a minute) for any of the four conditions, they were excluded from further analyses. However, no such extreme mean reaction times were found based on these criteria and no participant data were excluded from further analyses. All analyses were carried out using R programming.

Results

The performance of each birth experience groups on each task can be viewed in Figure 3 (VD and CSD) and Figure 4 (VD, emergency CSD and planned CSD). The hit and false alarm rates for each experimental group are presented in Table 1. Participants' performance in the TBT and their ability to discriminate between the task stimuli were evaluated using their *d*' scores.

Table 1

Hit Rates and False Alarm Rates of Each Experimental Group in Each Memory Condition

	Item-Recognition		Item-Item		Item-Space		Item-Time	
	Hit	FA	Hit	FA	Hit	FA	Hit	FA
	Rate	Rate	Rate	Rate	Rate	Rate	Rate	Rate
	M	M	M	M	M	M	M	M
	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)
Vaginally	0.81	0.25	0.70	0.49	0.74	0.36	0.69	0.39
born	(0.15)	(0.17)	(0.17)	(0.16)	(0.17)	(0.18)	(0.19)	(0.17)
C-section	0.80	0.24	0.70	0.49	0.78	0.32	0.72	0.37
born (E+P)	(0.13)	(0.19)	(0.15)	(0.19)	(0.16)	(0.18)	(0.18)	(0.23)
Emergency C-section born	0.81 (0.15)	0.17 (0.16)	0.73 (0.17)	0.42 (0.16)	0.81 (0.14)	0.29 (0.16)	0.76 (0.16)	0.32 (0.21)
Planned C-section born	0.80	0.28	0.67	0.54	0.77	0.34	0.70	0.41
	(0.12)	(0.19)	(0.13)	(0.19)	(0.17)	(0.19)	(0.19)	(0.24)

Performance (d') in Each Memory Condition

The performance of the two birth experience groups on the TBT was compared using a 2 x 4 two-way Mixed ANOVA with birth experience (VD and CSD) as the between-participants variable and memory condition (item-recognition, item-item, item-space, and

item-time) as the within-participants variable. No outliers were detected, as assessed by boxplot and the data was normally distributed, as assessed by Shapiro-Wilk's test of normality (p > 0.05). There was homogeneity of variances (p > 0.05) and covariances (p > 0.001) as assessed by Levene's test of homogeneity of variances and Box's M test, respectively. Mauchly's test of sphericity indicated that the assumption of sphericity was met for the two-way interaction ($\chi^2(5) = 2.25$, p = 0.81). The main effect of memory conditions was found to be significant (F(3, 237) = 39.95, p < 0.001, $\eta_p^2 = 0.34$). The main effect of birth experience, (F(1,79) = 0.41, p = 0.52, $\eta_p^2 = 0.005$) and the two-way interaction between birth experience and memory condition (F(3, 237) = 0.76, p = 0.52, $\eta_p^2 = 0.01$), were not significant, showing that the CSD group's performance did not differ from that of VD group's performance in the TBT.

To follow-up the main effect of memory condition, pairwise comparisons were conducted to compare d' scores for each condition across birth experience. All pairwise comparisons were run with 95% confidence intervals and p-values were Bonferroni-adjusted. The unweighted marginal means of performance scores were - item-recognition (M = 1.69, SE = 0.1), item-space (M = 1.2, SE = 0.1), item-time (M = 0.91, SE = 0.11) and item-item conditions (M = 0.56, SE = 0.08). Results showed that the participants performed significantly better in the item-recognition condition compared to all three relational conditions with a mean difference of 0.49 (95% CI [0.18, 0.8]) points higher than the item-space performance score, a mean difference of 0.78 (95% CI [0.48, 1.08]) points higher than the item-time performance score, and a mean difference of 1.13 (95% CI [0.85, 1.41]) points higher than the item-item performance score (all p's < 0.001). Comparing the three relational conditions, performance in the item-space condition was significantly better by a mean difference of 0.29 (95% CI [0.01, 0.58]) points than the item-time performance score and by a mean difference of 0.64 (95% CI [0.36, 0.92]) points than the item-item performance score.

Also, performance in the item-time condition was significantly better by a mean difference of 0.35 (95% CI [0.07, 0.62]) points than the item-item performance score (all p's < 0.05).

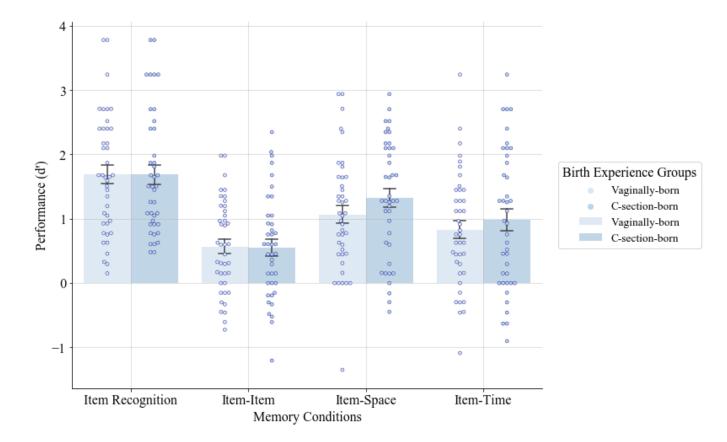


Figure 3. Performance of VD and CSD Adults in Each of the Triplet Binding Task Conditions. Error bars represent variability in standard error of means.

Planned comparisons were then conducted where simple between-subject contrasts were run for each of the memory conditions. This analysis did not reveal any significant mean differences in performance scores between the VD and CSD groups for item recognition (VD, M = 1.69, SD = 0.92; CSD, M = 1.69, SD = 0.95, p = 0.98, 95% CI [-0.42, 0.41]), item-space (VD, M = 1.07, SD = 0.89; CSD, M = 1.33, SD = 0.92, p = 0.2, 95% CI [-0.14, 0.66]), item-time (VD, M = 0.83, SD = 0.88; CSD, M = 0.98, SD = 1.08, P = 0.59, 95% CI[-0.29, 0.59]) or item-item (VD, P = 0.57, P = 0.57, P = 0.57, P = 0.55, P

Birth experience effects on relational memory were further investigated to check if there was a two-way interaction between birth experience and relational memory after dividing the CSD group into planned CSD and emergency CSD groups. A 3 x 4 two-way Mixed ANOVA was conducted where birth experience (VD, emergency CSD and planned CSD) was the between-participants variable and memory condition (item-recognition, itemitem, item-space, and item-time) was the within-participants variable. Extreme outliers were not detected, as assessed by boxplot and the data was normally distributed, as assessed by Shapiro-Wilk's test of normality (p > 0.05). There was homogeneity of variances (p > 0.05)and covariances (p > 0.001) as assessed by Levene's test of homogeneity of variances and Box's M test, respectively. Mauchly's test of sphericity indicated that the assumption of sphericity was met for the two-way interaction ($\chi^2(5) = 2.14$, p = 0.83). There was, once again, a significant main effect of memory condition on performance (d') in the TBT (F(3,234) = 34.19, p < 0.001, $\eta_p^2 = 0.31$) but no significant main effect of birth experience on performance (F (2, 78) = 2.23, p = 0.12, $\eta_p^2 = 0.05$) or interaction effects between birth experience and memory condition (F (6, 234) = 0.71, p = 0.64, η_p^2 = 0.02) were found, showing that the VD, emergency CSD and planned CSD groups did not perform differently from each other in any of the memory conditions.

To follow-up the main effect of memory condition, pairwise comparisons were conducted to compare d' scores for each condition across birth experience. All pairwise comparisons were run with 95% confidence intervals and p-values were Bonferroni-adjusted. The unweighted marginal means of performance scores were - item-recognition (M = 1.72, SE = 0.1), item-space (M = 1.25, SE = 0.11), item-time (M = 0.96, SE = 0.12) and item-item condition (M = 0.6, SE = 0.09). Performance in the item-recognition condition was significantly better compared to all three relational conditions with a mean difference of 0.47 (95% CI [0.14, 0.81]) points higher than the item-space performance score, a mean difference

of 0.76 (95% CI [0.44, 1.09]) points higher than the item-time performance score, and a mean difference of 1.13 (95% CI [0.83, 1.43]) points higher than the item-item performance score (all p's < 0.001). Out of the three relational conditions, performance in the item-space condition was significantly better by a mean difference of 0.66 (95% CI [0.35, 0.96]) points than the item-item performance score but item-space was not significantly better (mean difference of 0.29, (95% CI [-0.01, 0.6]) than the item-time performance score (p = 0.07). Also, performance in the item-time condition was significantly better by a mean difference of 0.37 (95% CI [0.07, 0.66]) points better than the item-item performance score (all p's < 0.05).

For planned comparisons, simple contrasts were run between the VD and emergency CSD group and were not significant for item recognition (VD, M = 1.69, SD = 0.92; emergency CSD, M = 2.01, SD = 1.07, p = 0.25, 95% CI [-0.86, 0.23]), item-space (VD, M = 0.25) 1.07, SD = 0.89; emergency CSD, M = 1.43, SD = 0.83, p = 0.17, 95% CI [-0.90, 0.17]), item-time (VD, M = 0.83, SD = 0.88; emergency CSD, M = 1.24, SD = 1.03, p = 0.16, 95% CI [-0.99, 0.16]) or item-item (VD, M = 0.57, SD = 0.71; emergency CSD, M = 0.9, SD = 0.90.88, p = 0.13, 95% CI [-0.76, 0.1]) conditions. Simple contrasts run between the VD and the planned CSD groups did not reveal any significant differences in performance either for item recognition (VD, M = 1.69, SD = 0.92; planned CSD, M = 1.47, SD = 0.82, p = 0.36, 95% CI [-0.25, 0.69]), item-space (VD, M = 1.07, SD = 0.89; planned CSD, M = 1.25, SD = 0.98, p = 0.980.42, 95% CI [-0.65, 0.28]), item-time (VD, M = 0.83, SD = 0.88; planned CSD, M = 0.8, SD= 1.1, p = 0.92, 95% CI [-0.48, 0.53]) or item-item (VD, M = 0.57, SD = 0.71; planned CSD, M = 0.32, SD = 0.67, p = 0.2, 95% CI [-0.13, 0.62]) conditions. Interestingly, the simple contrasts run between the emergency CSD and planned CSD groups did show a significant difference in performance in the item-item condition (see Figure 4) where the emergency CSD group performed better than the planned CSD group by a mean difference of 0.58 points (emergency CSD, M = 0.9, SD = 0.88; planned CSD, M = 0.32, SD = 0.67, p = 0.02, 95% CI

[0.11, 1.05]). However, there were no significant differences in performance between the planned and emergency CSD groups for item-recognition (emergency CSD, M = 2.01, SD = 1.07; planned CSD, M = 1.47, SD = 0.82, p = 0.08, 95% CI [-0.06, 1.13]), item-space (emergency CSD, M = 1.43, SD = 0.83; planned CSD, M = 1.25, SD = 0.98, p = 0.54, 95% CI [-0.40, 0.76]) or item-time (emergency CSD, M = 1.24, SD = 1.03; planned CSD, M = 0.8, SD = 1.1, P = 0.17, 95% CI [-0.19, 1.07]) conditions. This finding suggests that individuals born via emergency CSD can form more accurate item-item relational memories compared to those born via planned CSD.

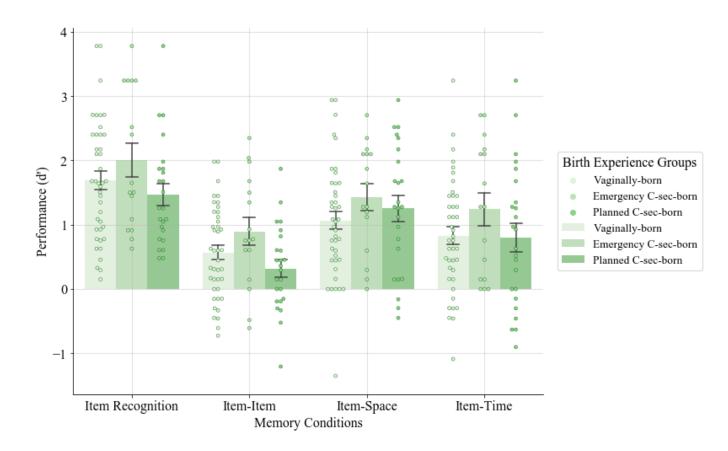


Figure 4. Performance of VD, Emergency CSD and Planned CSD Adults in Each of the Triplet Binding Task Conditions. Error bars represent variability in standard error of means.

Overall Relational Memory Performance (d')

An overall relational memory d' score was obtained as a measure of general relational memory functioning (see Figure 5). There were no outliers in the data, as assessed by

boxplot, the overall performance scores were normally distributed (Shapiro-Wilk's test p > 0.05) and there was homogeneity of variances as assessed by Levene's test for equality of variances (p = 0.38). To compare the overall relational binding performance between the VD and CSD group, a t-test was conducted. Results revealed that the mean difference of 0.12 in overall performance between the VD (M = 0.84, SD = 0.70) and CSD (M = 0.96, SD = 0.77) groups was not significant (t (79) = 0.74, p = 0.46, Cohen's d = 0.16, 95% CI [-0.20, 0.44]).

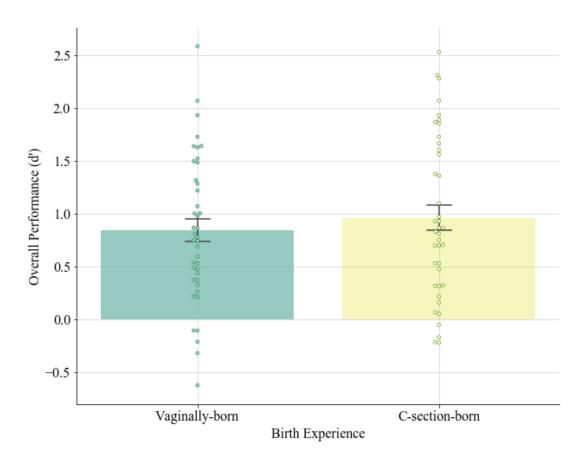


Figure 5. Overall Performance of VD and CSD Adults in the Relational Memory Task. Error bars represent variability in standard error of means.

Further analyses were performed with the sub-division of the CSD group into emergency CSD and planned CSD groups (see Figure 6). No outliers were found in the boxplot, the data was normally distributed (Shapiro-Wilk's test p > 0.05) and there was homogeneity of variances, as assessed by Levene's test (p = 0.21). An omnibus one-way

ANOVA was conducted with birth experience as the between-participant factor on overall relational memory performance. Estimates of marginal means showed that overall relational memory performance of the emergency CSD group (M = 1.23, SE = 0.18) was better than the VD group (M = 0.84, SE = 0.11), which was, in turn, better than the planned CSD group (M = 0.79, SE = 0.15), however, results revealed no significant differences in overall performance between the three birth experience groups (F(2, 78) = 2.1, p = 0.13, $\eta_p^2 = 0.05$).

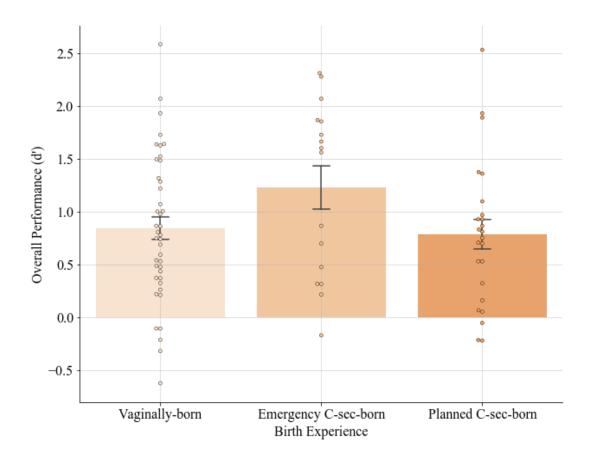


Figure 6. Overall Performance of VD, Emergency CSD and Planned CSD Adults in the Relational Memory Task. Error bars represent variability in the standard error of means.

Planned comparisons were conducted to compare the overall relational memory performance between each birth experience group. Simple contrasts run between the VD and emergency CSD groups (p = 0.07, 95% CI [-0.81, 0.04]), VD and planned CSD groups (p = 0.76, 95% CI [-0.31, 0.43]), and emergency and planned CSD groups (p = 0.06, 95% CI [-0.76, 95% CI [-0.76, 95% CI [-0.76]])

0.02, 0.91]) (VD, M = 0.84, SD = 0.7; emergency CSD, M = 1.23, SD = 0.82; pl. CSD, M = 0.79, SD = 0.69) were not statistically significant.

From the above results, birth experience, specifically being born through planned CSD, seems to significantly affect the formation of item-item relational memories and not item-space or item-time relational memories compared to being born through emergency CSD. Moreover, participants' performance in the TBT shows that item-item binding seems to be more difficult compared to item-time or item-space binding.

Discussion

The birth of an organism is the most crucial aspect of its life. The events leading to the birth of an organism, including humans, can influence their development (Arteni et al. 2003; Kalpakidou et al., 2012; Modir et al., 2014). Yet, the number of studies that report the effects of birth experience on human cognitive and brain development are very few, with little to no studies reporting about birth experience effects lasting into adulthood. The few studies that have reported any such effects include attentional differences found between CSD and VD infants (Adler & Wong-Kee-You, 2015) and adults (Rahimi & Adler, 2019; Stevens, Adler, et al. (under review)). The commonly shared brain regions between attention and episodic memory processes (Cabeza et al., 2003) and the fact that memory and attention cannot operate without each other (Chin & Turke-Brown, 2007; Craik & Lockhart, 1972; Lockhart & Craik, 1990; Wolfe, 2021) brings into question whether birth experience also affects a critical component of episodic memory, that is, relational memory and if it manifests in adulthood (Olson & Newcombe, 2014). Relational memory enables us to remember the events in our life by connecting an event's elements, a process called binding. If the development of relational memory is disrupted by factors such as birth experience, not only would it affect the integrity of the episodic memories formed but also the implications of

binding on processes like making associations between our past, present, and future states (Coughlin et al., 2014) and forming autobiographical memories (Nelson & Fivush, 2004). No studies to date have investigated if the attentional differences found between CSD and VD adults (Rahimi & Adler, 2019; Stevens, Adler et al. (under review)) extend to associated higher-order cognitive functions such as relational memory.

In the present study, therefore, the effects of birth experience, that is, whether being born via CSD or VD, on relational binding operations were examined in adults. The effects of the type of CSD, that is, whether being born via planned CSD or emergency CSD, on relational memory were examined as well. These effects were studied by using a paradigm that involved testing item memory and the three types of binding operations, (item-item, item-space, and item-time). Data from the three relational memory types were combined and assessed as a measure of how overall relational memory could be affected by birth experience as well. Two of the findings were consistent with the predictions made for the present study.

One of the findings was that the adult participants overall were able to form itemspace relations and item-time relations better than item-item relations which was consistent with previous studies that reported the same finding (Konkel et al., 2008; Lee et al., 2015). Moreover, the result that item-space performance was better than item-time performance was contradictory to that of previous studies that found no differences between adults' performance in the item-space and item-time condition in the TBT (Konkel et al., 2008; Lee et al., 2015). However, this finding is consistent with other studies that have found that adults' overall accuracy in remembering spatial relations is better than that of temporal relations (Dutta & Nairne, 1993; Pathman et al., 2018). Overall, the differences in performance across the three relational conditions suggests that there may be some hierarchical organization in our memories such that item-space relations are better retained

than item-time relations (Pathman et al., 2018), and both item-space and item-time relations are better retained than item-item relations (Lee et al., 2015).

The second finding of the present study was that adults born via planned CSD were significantly less accurate in forming item-item relations compared to adults born through emergency CSD. However, there were no significant differences between the planned CSD and VD groups, or the emergency CSD and VD groups. These results regarding birth experience influences on relational memory can be explained by certain mechanisms that could have operated behind the formation and retrieval of such memories.

Attentional Mechanisms

In the current study, adults' performance in an item-item memory condition was found to be significantly poorer compared to item-space or item-time conditions. More importantly, decreased performance in the item-item memory condition in the planned CSD groups compared to the emergency CSD group was significant, but the planned CSD group did have a lower mean performance score than the VD group though it was not significant. One explanation for the influence of birth experience on item-item binding could be due to differences in the operation of attention-related mechanisms in the different birth experience groups as previous studies found that birth experience affects visual attention in adults (Rahimi & Adler, 2019), a cognitive function which is closely related with memory (Chun & Turk-Browne, 2007; Craik & Lockhart; 1972; Lockhart & Craik, 1990; Wolfe, 2021).

For episodic events to be efficiently encoded, attention to each event is necessary along with efficient processing of the details of the events (Craik & Lockhart, 1972). Though memory tasks involving object recognition generally require top-down attentional allocation, every task however also activates bottom-up attention to process any unexpected features of task stimuli (Wolfe, 1994; Wolfe, 2021). In the TBT, for example, participants had to

selectively allocate their attention to details such as each of the images in a triplet, its spatial location, when it appeared in time, and which triplet it belonged to. Bottom-up attentional resources could have been used more than top-down attentional mechanisms when the novel visual stimuli were shown one after the other for the first time as participants did not know what their target object would look like leading to the processing of basic features of each of the items such as their color combination, shape and orientation (Wolfe, 2021). The presentation of the triplet sequences a second time could have then led to the use of the top-down guiding template present in working memory (Wolfe, 2021) to deploy attention to the relevant details of the items. In other words, any encoding of the item and relational information that may have occurred due to activation of stimulus-driven bottom-up attention when stimuli were shown the first time could have led to expectations of when and where the stimuli would appear next when the triplet sequences were shown again a second time, thus, activating goal-driven top-down attention.

Processing of the multiple features of the stimuli could have also occurred differently depending on the relations to be encoded. In the item-space and item-time conditions, features such as the image location and its ordinal position in a triplet could have been processed more easily as this information was provided simultaneously to the presentation of the image and a bound representation of each of the images could have been created with these features. In contrast, the item-item condition involved connecting images appearing serially one after the other and in distinct locations on the screen, which could have made the process of selective allocation of attentional resources and encoding more difficult as multiple features of each of the three items in a triplet are now held in working memory (Wolfe, 2021) along with the information of the images in the other triplets in an encoding phase. Moreover, relating the items may not have been possible unless some semantic connection between the items was made to remember each of them in the triplet such as

similar shape, similar color, or any such strategy the participant may have used while trying to encode the relations between the novel images. This could have required deeper processing than the item-space or item-time conditions (Craik & Lockhart, 1972; Lockhart & Craik, 1990), making the item-item condition the most difficult one among the three relational conditions. As a result, item-item relations could have been harder to retrieve during the recognition test compared to the item-space or item-time conditions if they were not accurately encoded in the first place.

Since stimulus-driven reflexive attention was found to be slowed in adults born via CSD (Rahimi & Adler, 2019), they may not have been able to allocate adequate attention to all details within the limited encoding time given for each image in the TBT. Perhaps the time to shift attention from one image to the next one was enough to accurately encode only spatial and temporal relations but not enough to form semantic associations between the images that constituted a triplet, even with the presentation of triplet sequences a second time. This could be why significant differences between the birth experience types were found in the item-item condition and not in the item-space or item-time conditions. In the current study, the planned CSD group had decreased ability to bind item-item relations than the emergency CSD group which could have been due to attentional mechanisms being more impacted by planned CSD such that adults in this group may not have had enough time to elaborately process the item-item relations in a triplet to accurately retrieve them. Furthermore, the above novel finding suggests that there are relational memory differences between adults born via planned CSD and emergency CSD due to attentional differences existing between these groups in adulthood. This claim, however, is contradictory to Rahimi and Adler's (2019) suggestion that the difference in reflexive attention found between planned and emergency CSD groups in infancy minimizes with age and becomes nonexistent in adulthood. The different tasks used, and the goals of the two studies could have

brought about this inconsistency. For instance, visual attention was measured in the study by Rahimi and Adler (2019) using a search asymmetry task, but the current study measured relational memory using the TBT which would have been much more difficult and taxing on the attentional system in adults. In conclusion, slower attentional allocation and inadequate processing of item-item relations between the images in a triplet may have resulted in poor encoding in the first place, thus, leading to decreased performance in the item-item condition in the planned CSD group compared to emergency CSD and VD groups.

Attempt to Bridge Spatiotemporal Gaps

Another possible explanation for differences in performance in the item-item binding condition compared to the other two relational conditions is the attempt to bridge spatiotemporal gaps while forming item-associative memories (Staresina & Davachi, 2009). Associative memories are formed due to long-term potentiation (LTP) of the postsynaptic response and, potentiation of synaptic transmission occurs when two neurons co-activate within ~ 100 ms (Levy & Steward, 1983). As a result, memory sequences are thought to be encoded when the sequential events have a temporal separation of < 100 ms (Wallenstein et al., 1998). If the temporal separation is larger than this time window of 100 ms, the encoding of such sequences is suspected to be dependent on a memory buffer, such as that provided by the hippocampus, that can extend the active firing of neurons for many more seconds to encode the associations between the events. Computational models proposed by Lisman (1999) and Wallenstein et al. (1998) along with findings from Staresina and Davachi (2009) with adult human participants found that bridging such separations or gaps between representations of spatial and temporal events involves the active engagement of the hippocampus and the larger the gap, the more the hippocampal engagement. If this is the general process that occurs while forming item-item memories, theoretically, accurately connecting separate events and distinguishing between them may be affected if the

development of the neural substrate for these processes, that is, the hippocampus, is affected. Moreover, the ability to distinguish between the features of an episode and across episodes is speculated to be supported by specific populations of hippocampal neurons such as time cells in the CA1 regions and pyramidal cells (MacDonald et al., 2011) of the CA3 regions (Lisman, 1999; Wallenstein et al., 1998).

In the current study, triplets separated by an inter-trial interval of 1000 ms could have created such spatiotemporal gaps in representations of the image sequences requiring not only the participants to remember and distinguish between the items within an episode, that is, the presentation of images within a triplet, but also across the episodic boundaries, that is, across the four triplets presented in an encoding phase. Considering that animal models (Castillo-Ruiz et al., 2018; Chiesa et al., 2018; Huang et al., 2019) found hippocampal regions like CA1 and CA3 sub-fields to be affected by CSD, the subsequent development of these regions may have been affected, impacting their function of bridging spatiotemporal discontiguities in adulthood. If this is true, adults born via planned CSD in the current study may have possibly found more difficulty in encoding and distinguishing between items shown within and across triplets in the item-item condition. The above explanation, however, is purely speculative. Focused research on comparing item-item binding across different spatiotemporal gaps and stimulus durations along with neural measures to test the level of hippocampal engagement between different birth experience groups in adults may be able to verify if these mechanisms are in fact, affected by being born via planned CSD and have long-term consequences.

Birth-Related Mechanisms

Other plausible explanations behind the differential performance in the relational memory task across the different birth experience groups are 'bacterial baptism' or

experience of maternal labor-induced changes that have been theorized to affect brain-related mechanisms and consequently cognitive development (Polidano et al., 2017).

Bacterial Baptism Theory

The 'bacterial baptism' theory proposes that passing through the vaginal canal initiates the seeding of the gut microbiome in the neonate which plays a crucial role in forming a microbiota-gut-brain axis to communicate with the central nervous system (Cryan & Dinan, 2012). VD infants are initially exposed to bacteria through the vaginal canal (Bezirtzoglou, 1997) whereas infants born through CSD are deprived of this early opportunity for the seeding of the gut microbiome. The seeding, however, may occur later after birth from exposure to bacteria in the hospital environment, the mother's skin, breastmilk, or healthcare workers (Grölund et al., 1999; Polidano et al., 2017). Recently, studies have found that gut microbacteria can communicate with the central nervous system through chemical signals (Cryan & Dinan, 2012; Galland, 2014) and that brain development is linked to adequate functioning of the gut microbiome (Borre et al., 2014; Collins et al., 2012; Gareau, 2014). A disruption in microbiota composition might therefore affect subsequent brain development and cognitive functions such as memory and attention.

More recently, studies have found that CSD could lead to disturbed gut microbiota which, in turn, was found to be associated with negative consequences on the cognitive and behavioral systems that are suspected to last long-term (Polidano et al., 2017). For example, decreased levels of brain-derived neurotrophic factor (BDNF) and decreased expression of the NMDA receptor subunit in the cortex and hippocampus were associated with disturbed gut microbiota (Sudo et al., 2004). BDNF is associated with neuronal growth and survival (Bathina & Das, 2015) while hypofunctioning of NMDA receptors has been associated with deficits in memory (Newcomer et al., 2000). Moreover, germ-free animals showed deficits in

memory tasks involving novel object recognition and spontaneous alternations in the T-maze (Gareau et al., 2011), and had elevated hippocampal concentrations of 5-hydroxytryptamine (5-HT) which has not only been shown to regulate the serotonergic system (Clarke et al., 2012) but also has been associated with memory impairment and depression (Meeter et al., 2005). Even when the germ-free animals were colonized with bacteria post-weaning, peripheral tryptophan levels were restored but did not reverse the changes in serotonin levels in the CNS in adulthood due to absent microbiota early in life (Clarke et al., 2012) suggesting that the consequences of disturbed gut microbiota on the brain at birth may not fully recover.

The disturbance in the gut microbiome composition due to CSD could have, therefore, led to a delay in attentional systems, as speculated by Rahimi and Adler (2019), and consequently to a delay in memory development or could have directly impacted the memory systems by affecting BDNF (Sudo et al., 2004) and 5-HT levels (Clarke et al., 2012) in the hippocampal region which is responsible for relational memory. Put together, these explanations suggest that the decreased performance of the planned CSD group in the itemitem memory condition compared to the emergency CSD group could have been due to comparatively delayed seeding of the gut microbiome in the planned CSD group which could have consequently led to shortfalls in their development of cognitive processes such as relational memory. Also, the disrupted microbiome speculated to impact brain development more slowly and over a longer period (Polidano et al., 2017) could have made such differences between the planned and emergency CSD groups apparent only in adulthood, or even earlier but this can only be confirmed with future studies. The non-significant differences between the emergency CSD and VD groups, however, do not align with this explanation as the emergency CSD group, presumed to also have disturbed microbiota, should have shown decreased performance in the TBT compared to the VD group. An alternative explanation to this lack of a difference is that partial maternal labor-induced

benefits, as will be discussed next, could have provided a boost in terms of cognitive development, thus counteracting any long-term negative effects of a disturbed gut microbiome in the emergency CSD group.

Maternal Labor-Induced Changes

The stress of birth is said to induce many changes in the neonate's body and brain as a response to immune challenges, hypoxia and the mechanical squeezing of the head for several hours during labor (Lagercrantz, 2016; VanWoudernberg, 2012). According to the "birth process" theory illustrated by Toda et al. (2013), labor and traversing the birth canal is thought to cause a decline in serotonin levels, consequently triggering an acceleration in development of specific brain regions that use serotonin. This was observed in rat pups that showed differences in their brain development when the rat mothers or dames were induced to give birth prematurely. The stress of birth caused an accelerated development in the cortical barrel formation of rat pups postnatally (Toda et al., 2013) which has been traced to its corresponding brain region in humans, the somatosensory cortex, involved in reactive spatial attention (Balsey et al., 2013; Jones et al., 2010). If this "birth process" is not experienced by certain individuals, like those born via CSD, there may be implications to attentional development and consequently to the development of connected cognitive functions like memory. As planned CSD individuals do not experience the "birth process", their development of visual attention mechanisms is likely to be affected and this was supported by findings from Rahimi and Adler (2019) where visual attention was slowed in this group of infants and adults compared to emergency CSD or VD adults. As a result, the development of memory, a connected cognitive function could have been affected and could be why the planned CSD adults in the current study had decreased ability to form item-item relational memories compared to emergency CSD or VD adults that do undergo the "birth process".

Other neurochemical responses like UCP2 (Seli & Horvath, 2013; Wang et al., 2014) and glucocorticoid expression (Huang et al., 2019) in the hippocampus play a role in neuronal growth and differentiation and learning and memory which was found to be decreased in CSD mice. Also, vasopressin release has been associated with a reduction in neuronal cell death in VD mice compared to CSD mice (Hoffiz et al., 2021). Considering that individuals born via planned CSD do not undergo any maternal-labor-induced stress, neuronal cell death could be prolonged in certain brain areas, thus causing developmental delays in cognitive function. Since the dentate gyrus, CA1 (Castillo-Ruiz et al., 2018), and CA3 sub-regions (Chiesa et al., 2018) were found to be impacted due to CSD birth in mice, the same human hippocampal sub-regions may similarly be impacted due to lack of maternal-labor-induced benefits. Moreover, the development of the CA3 subfield and the dentate gyrus is protracted compared to the rest of the hippocampus (Lavanex & Lavanex, 2013), and these regions are related to item-associated binding (Lee, Ekstrom & Ghetti, 2014; Leutgeb & Leutgeb, 2007; Rolls, 2013). Early experiences such as planned CSD, could have affected these hippocampal regions, in turn, affecting the ability to bind item-item relations in the long-term which could be why the planned CSD adults showed decreased performance in the item-item condition compared to emergency CSD and VD groups in the present study.

Interesting to note was that the emergency CSD group performed best in all four conditions and in overall relational memory performance compared to the planned CSD and VD groups (as can be seen in Figures 4 and 6). This was contradictory to the initial prediction that the VD group would perform better than either of the CSD groups. A possible explanation for this observation is that the individuals born through emergency CSD undergo the effects of partial maternal labor and may still benefit from stress-induced endocrine responses that could prevent neuronal cell death and accelerate the development of brain regions responsible for visual attention, thus leaving memory development relatively

unaffected. The later seeding of the gut microbiome from the mother's skin and the hospital environment, combined with the partial labor-induced benefits could minimize any shortfalls associated with CSD, or as found in this study, even aid in forming more accurate relational memories compared to VD adults. However, these results between emergency CSD and VD adults were not significant and need to be verified with follow-up studies on how the types of birth experience affect memory at different stages of development using both neural and behavioral measures.

The above theories, however, do not explain why there were no significant differences in performance between the planned CSD adults and the VD adults in the item-space, itemtime or item-item conditions. Though the mean performance score is higher for the VD group for the item-item condition compared to the planned CSD group as expected, they are almost equal for the item-space and item-time conditions. One possible reason for this is that there are age-related improvements in relational memory formation. For example, item-space binding reaches adult levels by approximately 9 years of age, item-time binding abilities reach adult levels by approximately 11 years of age (Lee et al., 2015; Riggins et al., 2018) and item-item memory develops well into adolescence and young adulthood (Lee et al., 2015). Even if planned CSD had delayed the development of item-space or item-time relations, both binding processes would have reached adult levels well before young adulthood. Perhaps any differences in item-space or item-time relational memory due to planned CSD could have existed only around the time of 9 or 11 years of age respectively, but such differences may have minimized over time as planned CSD individuals caught up with VD individuals and could have ultimately ceased to exist in adulthood. For the itemitem condition, the higher mean performance scores of the VD adults compared to planned CSD adults, though not significant, could imply that the development of item-item relations in the planned CSD groups is either in the process of catching up to the VD group in planned

CSD adults compared to the VD adults or the ability to bind item-item relations is just permanently affected by planned CSD.

Another reason why birth experience differences might not have emerged is because of the online nature of task administration that differed from previous studies that had used the TBT offline (Konkel et al., 2008; Lee et al., 2015; Ring et al., 2015) and from previous studies that explored birth experience differences in human cognition by administering their tasks in person (Adler & Wong-Kee-You, 2015; Deoni et al., 2018; Stevens, Adler et al., (under review); Rahimi & Adler, 2019). The online administration of the task gave little control over the participant's testing environment. Though the entire process of the TBT was supervised using Zoom, control over factors such as the participant's seating posture, the distance between the participant and the screen, background noise, lighting and different computer or laptop screen sizes and resolutions used by different participants were very limited. Previously, a study comparing online testing and in-person testing of the same psychological assessment found that people tend to score lower on the online test (Vallejo et al., 2007) but other studies have found online testing to be a valid tool for the cognitive assessments used in their studies (Germine et al., 2012; Ashworth et al., 2021). These contradictory findings may be due to the different assessments used in the study and variation in the level of appropriateness of online administration of the chosen task. A comparison should, therefore, be conducted between online and offline administration of the TBT to check if the birth experience effects on relational memory vary with the nature of task administration.

Overall, as predicted in the present study, there were differences between the emergency and planned CSD groups, specifically, planned CSD adults had decreased ability in forming item-item relational memories compared to emergency CSD adults and the average performance of all adult participants in the item-item condition was poorer compared

to the item-space and item-time conditions. CSD in general, however had no effects on relational memory in adulthood. The findings of the present study suggest that birth experience effects on relational memory could have been carried over from birth experience differences found in attentional mechanisms and on underlying brain regions responsible for relational memory. The findings also lend credence to both birth-related theories in terms of how disturbances in physiological and neurochemical mechanisms due to planned CSD could affect subsequent cognitive development.

Future Directions

The current findings inspire the need to ask more questions regarding the role of birth experience in cognitive development. First, the online nature of the study could have led to unidentified findings regarding birth experience, therefore, the TBT could be administered in person with more control over extraneous variables to observe the effects of birth experience on relational memory and if they vary from the results found with online administration of the TBT. Second, the potential effects of other gestational and birth-related variables need to be assessed along with birth experience such as the infant's gestational age and weight (Barber et al., 2011; Gutbrod et al., 2000), drugs given during gestation (Sachdeva, Patel & Patel, 2009), maternal weight (Chu et al., 2007), and the method of feeding that the mother used (breastfeeding or bottle-feeding) (Belfort, 2017) that could together play a role in memory development since these factors have been found to affect brain development. Third, the differences in the ability to form relational memories due to birth experience should be tracked across ages like during infancy, early and late childhood, and adolescence to verify if the birth experience differences in memory performance are observed in childhood as well. Lastly, focused research on memory tasks that require differential recruitment of top-down and bottom-up attentional mechanisms could inform how attentional resources are allocated while forming relational memories. More interesting to observe would be potentially different levels of recruitment of brain areas, like the hippocampus, MTL, and the frontoparietal network that is active for both attention and episodic memory tasks (Cabeza et al., 2003; Guillery-Girard et al., 2013), across different birth experience groups while performing a relational memory task.

Conclusion

CSD is a necessary surgical process performed when any complications arise during gestation or during birth that signals that the survival of the mother and infant is at risk but in the past few decades, the number of CSD births have risen globally at an alarming rate (World Health Organization, 2021) with an increase in CSD births on maternal request after 2010 (Begum et al., 2020). Consequently, there is a need to understand if CSD has potential negative outcomes on human cognitive development and whether these effects are long-term. The present study, therefore, addressed this question and found that birth experience affects the ability to form relational memories, specifically item-item memories. These effects were found with adult participants showing that the events leading to birth have long-term consequences on memory. Furthermore, planned CSD was found to negatively affect the ability to form some relational memories compared to emergency CSD. These findings must be noted so that healthcare professionals and expecting mothers are informed about the psychological implications on the neonate along with a host of other previously identified physiological ones associated with caesarean section delivery.

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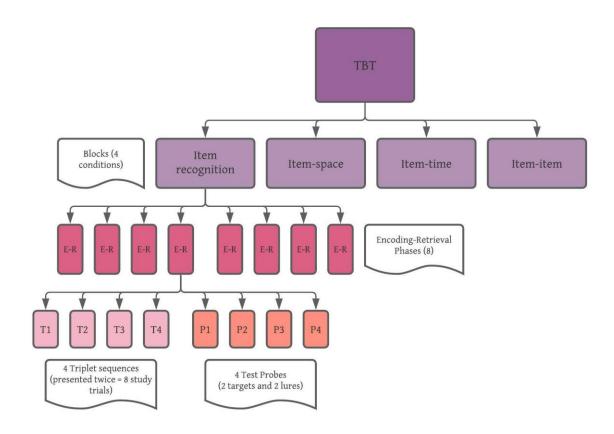
World Health Organization. (2021, June 16). *Caesarean section rates continue to rise, amid growing inequalities in access: WHO*. World Health Organization.

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Appendices

Appendix A: Task Design Schematic

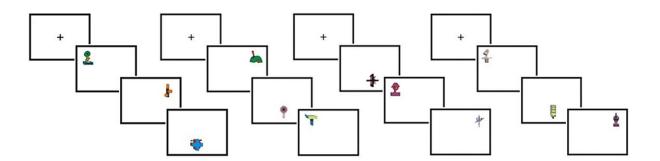


Appendix B: Instructions for Participants

Welcome! This is a memory test called the Triplet Binding Task. You will be presented with 4 triplets for every study phase and then a series of questions will be asked about the images. Each of the images will be presented one at a time in three distinct locations – top left, top right or the bottom middle of your screen. Between each triplet, a white screen will appear with a fixation cross. Please pay attention to:

- 1. Each of the images
- 2. The set/triplet the images belong to
- 3. The image locations
- 4. The order of appearance of images

The four triplets will be shown twice in every study phase.



Following the presentation of the image sequences, a screen will appear with three images for a few seconds and then go off. You will then be presented with a question and two options "Yes" or "No".

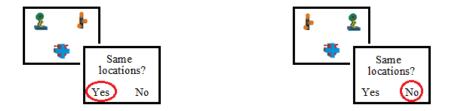
i) If the question you see says "Previously seen?" - select "Yes" if the three images you saw in the preceding screen were the same ones you saw in the study phase. If even one of the three images is new, select "No". The task will not progress until a response is selected.



ii) If the question you see says "Same group?"- Select "Yes" if the three images you saw in the preceding screen belonged to the same triplet. If even one of the three images do not belong in that triplet group, please select "No". The task will not progress until a response is selected.

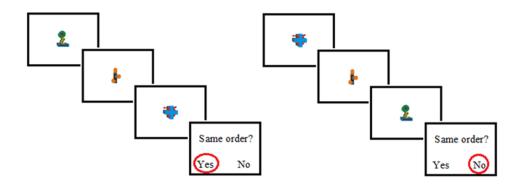


iii) If the question you see says "Same locations?"- select "Yes" if the three images you saw in the preceding screen were in their same respective locations as seen in the study phase. If even one of the three images has changed its original location, select "No". The task will not progress until a response is selected.



iv) If the question you see says Same order?" - Select "Yes" if the three images you saw were presented in the same sequence (1st, 2nd, or 3rd in the sequence) as seen in the study phase. If even one of the three images has

changed its ordinal position, select "No". The task will not progress until a response is selected.



First, you will receive a practice session to understand the procedure described above after which the actual task will begin. The researcher will re-instruct you about the procedure if required. You can also clarify any doubts you have about the procedure with the researcher after the practice session.