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Visual attentional control in neurotypical adults and children with ADHD

Ву

RAISA AMAL RAHIM

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

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Abstract:

Attention as an umbrella term covers a vast array of topics. In **Chapter 1**, we review the relevant background on selective attention, as it is a vital function for humans to navigate the stimulus-rich environments they are immersed in and how it relates to object recognition. In **Chapter 2**, we explore the role of target templates that are powerful heuristics for integrating remembered concepts with novel percepts in a task-efficient manner. Target-distractor similarity and linear separability have previously been shown to moderate properties of the target template representation in memory for unidimensional objects; we sought to extend these findings in multidimensional objects (each dimension of which was independently manipulated) by recruiting participants to perform simultaneous visual search and memory probe tasks. Results showed that target-distractor similarity moderated search efficiency and was associated with an off-veridical memory bias and an altered method of extracting information. And in **Chapter 3**, we review established and experimental interventions for children and adolescents with attention deficit/ hyperactivity disorder to improve this population's wide array of atypical and adverse symptoms, including selective attention deficits.

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Chapter 1:

General Background

The real-world environment offers an exponential amount of stimulation, with the potential to overwhelm our senses. Attention covers a broad swath of abilities relying on a broad range of neural systems (Hommel et al., 2019). There is thus a wide variety of capacities and affected populations loosely tied to this umbrella term.

Selective attention (SA) allows us to detect relevant information while ignoring irrelevant information so that we can efficiently engage in task-oriented behavior. The transiently activated and expectation-influenced target template is a critical mental representation to perform this function effectively and flexibly (Grubert & Eimer, 2018), as it provides both guidance for how to implement top-down processing and a comparison to match to while doing bottom-up processing (Geng & Witkowski, 2019; Hout & Goldinger, 2015). It is moderated by external factors like stimulus frequency (Rich et al., 2008) and internal factors like expectations given prior knowledge (Malcolm & Henderson, 2009).

The template's proper functioning relies on interaction with several other cognitive capacities to further process the attended information. Given that target templates are a mnemonic device (Huynh Cong & Kerzel, 2020), SA heavily relies on mnemonic function for successful execution of tasks (Summerfield et al., 2006). Working memory is a particularly crucial counterpart, as their interaction supports flexible representations of the dynamic, multimodal stimulus space (Lau et

al., 2019). While SA may be processed in any single sensory modality or in multiple modalities, we will here focus on how attention modulates perception given various properties of visual stimuli.

Neural basis: This class of cognitive processes relies on the interplay among several neural substrates, the most characteristic complex being the frontoparietal network (FPN). As this constellation of substrates is also known as the dorsal attention network, it hosts many regions important for visual orienting. Cortical regions like the frontal eye fields and the intraparietal sulcus have been shown to be necessary cogs in the saccade orienting mechanism (FEF, IPS; Wei et al., 2011). Given the interplay between the dorsal and ventral attention networks (*Figure 1*), visual orientation is paired with stimulus property processing (Vossel et al., 2013; Lee & Geng, 2016). Specifically, when an object is fixated upon, substrates like the temporoparietal junction and the ventral frontal cortex support processes like contextual updating and cognitive control in response especially to unexpected stimuli in the dynamic environment, respectively (TPJ, VFC; Geng & Vossel, 2013; Vossel et al., 2013).



<u>Figure 1:</u> Functional and neuroanatomical connections between the dorsal (frontoparietal) and ventral (occipitotemporal) attention networks. Figure taken from Vossel et al. (2013).

With input from target template processing areas, the system is equipped to navigate the environment efficiently. The dorsal attentional network can discriminate the target from its distractors (Ischebeck et al., 2021), where target template representations reflect expectation in a manner that optimally distinguishes the two stimulus classes (Grubert & Eimer, 2023; Yu & Geng, 2021). Representation similarity analyses of these templates revealed distinct activation patterns during search for feature conjunctions according to processing stage (Reeder et al., 2017); broad regions of frontal, occipitotemporal and posterior parietal cortices differentially activated during stimulus maintenance over a delay period by task relevance, while frontal and occipital poles did so at stimulus encoding.

<u>Visual search</u>: Visual search is a fundamental ability based on SA. Building upon the foundational work of Broadbent (1956), this has led to several further investigations into SA's mechanism of action. One of the most prominent models of visual search as it relates to object recognition is Treisman and Gelade (1980)'s feature integration theory which put forward that individual features are processed automatically and in parallel at a preattentive stage, with feature conjunctions processed serially at a later stage. As this theory's clean delineations between attentional stages may not reflect all realistic search dynamics (Wolfe, 2020), Jeremy Wolfe (Wolfe et al., 1989; Wolfe, 2021) outlined the processes underlying visual search, progressively integrating more components that modulate perception of the visual environment (Wolfe, 2021; *Figure 2*).



<u>Figure 2:</u> Guided Search 6.0, a revised model of SA deployment to facilitate object recognition. Figure taken from Wolfe (2021).

Once the sensory stimuli are transduced by the visual system, the "gist" of the sensoria is encoded in a single feature dimension, perhaps as it has not yet gained the template status that affords the percept greater precision (Rajsic et al., 2017; Won & Geng, 2018). After then passing through a 'bottleneck', the individual features are re-bound into feature conjunctions and compared to target and distractor templates that are flexibly held in working memory. Using prior knowledge of stimulus context organized as priority maps that guide search (Phelps et al., 2022), the object recognition can be made once the template match is decided upon.

Object recognition success can be modulated in the presence of several visual properties. As mode of presentation has been shown to affect depth of processing (Brady & Störmer, 2022), search dynamics are affected by several perceptual properties of the stimuli (target prevalence, featural salience; Rich et al., 2008; Stilwell et al., 2019). In particular, target-distractor differences

play a crucial role in moderating the efficiency of task-related behavior (Geng et al., 2017; Delvenne & Dent, 2008; Yu et al., 2022).

By the feature similarity gain model (Martinez-Trujillo & Treue, 2004), feature-based attention increases neuronal selectivity to favor selection of the target feature. Becker (2010) showed that feature similarity is perhaps not the most important characteristic, as feature relations between a target and its distractors may take precedent. This led Geng and colleagues (2017) to investigate this linear separability effect further, finding that this property produced a target template representation shifting effect in memory that exaggerated target-distractor differences as an adaptation to facilitate search. Further, it was the target-distractor similarity of the stimuli producing this 'off-veridical' mnemonic bias that moderated the precision of the target template (*Figure 3*; Yu & Geng, 2019).



<u>Figure 3:</u> Target template representation modulation. The proportion of 'target yes' responses were computed in response to various levels of target-distractor and distractor-distractor similarity and linear separability. Figure adapted from Yu & Geng (2019).

Becker, Atalla, and Folk (2019) had participants view a series of search arrays containing colorsize conjunctions in search for a target feature conjunction. Depending on the distractors presented, each feature dimension could be searched for by either a feature-specific or relational heuristic (harnessing target-distractor similarity or linear separability, respectively). For example, in search for the medium aqua target, it would be adaptive to search for a large aqua when distractors were smaller and a terminal color (green or blue). In this case, whereas the target color would be an ambiguous color at the intersection of these color categories, the target size had a feature at an unambiguous, endmost value. The target color was not linearly separable from distractors, but size was. This would ideally require the use of a feature-specific heuristic to select color and a relational heuristic for size. Since the stimuli used were not constrained such that stimulus color was associated with stimulus size, these results suggest that different dimensions can be independently and simultaneously searched for using different heuristics. This informs how illusory conjunctions may arise in relation to the feature binding problem (Li et al., 2022).

<u>*Clinical implications:*</u> Several clinical populations exhibit deficits in selective attention employment. In adults with clinical depression, patients show moderate deficits in SA such that their taskoriented efficiency is low (Semkovska et al., 2019). Patients with schizophrenia exhibit hyperfocusing tendencies, in which they struggle to disengage and shift attentional control along with dynamic task demands (Hahn et al., 2022).

Attention deficit/ hyperactivity disorder (ADHD) is a highly prevalent disorder, with a growing body of American children receiving this diagnosis (Schnorrbusch et al., 2020; Bitsko et al., 2022). These patients exhibit a wide range of symptoms, including deficits in SA (Mason et al., 2003; Mullane & Klein, 2008). While performing visual search tasks, they show deficits in target recognition accuracy but not in speed of response (Hokken et al., 2023); this search accuracy effect was further corroborated when examining children's discrimination abilities (Fernández-Andrés et al., 2019).

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Chapter 2:

Adaptive target template tuning for multidimensional stimuli tracks relational and featural targetdistractor distinctiveness

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Abstract:

How objects are represented in memory to facilitate target recognition is still unclear, especially when the target is defined by multiple feature dimensions. Target-distractor similarity and linear separability are properties known to modulate stimulus distinctiveness. Using a counterbalanced design, we independently manipulate each of these factors in the Shape and Color dimensions as participants perform visual search and memory probe tasks. Results showed an association between target-distractor similarity and linear separability that is moderated by dimension-specific properties of the distractor context to affect how target search is executed. Implications and future directions are discussed.

<u>Keywords:</u> target-distractor distinctiveness, visual working memory, visual search, target templates

INTRODUCTION:

The visual world is filled with more stimuli than can be efficiently perceived. In search for a target object among this overabundance of sensory input, search templates held in working memory guide attention to facilitate target recognition in a task-relevant manner (Kong et al., 2020). This template must be able to distinguish the target from non-targets (Geng & Witkowski, 2019). How discriminability relates to memory precision remains unclear, though several previous studies have found that the template holds a representation that is optimal, not strictly veridical, for creating target-distractor distinctiveness (Navalpakkam & Itti, 2007; Scolari & Serences, 2009; Yu & Geng, 2019). The precision with which these search templates are held in working memory varies depending on the makeup of the context (Lau et al., 2019; Won et al., 2021).

Several heuristics may be employed to increase target-distractor discriminability (*Figure 1*). The most well-studied way in which target-to-distractor distinctiveness can be increased is through decreasing target-distractor similarity (*Figure 1A;* Treisman & Gormican, 1988; Duncan & Humphreys, 1989). Decreasing the similarity between stimuli increases the signal-to-noise ratio between target and distractor template representations (Maunsell & Treue, 2006; Scolari et al., 2012). However, when discrimination is difficult, i.e. when target-distractor similarity is high, cognitive manipulations shaped by top-down processing, rather than automatic perceptual consequences of target-distractor linear separability (*Figure 1B,C;* Becker, 2010; Rosedahl & Ashby, 2021; Soto et al., 2008) are used to facilitate search. Target template representation shifting and asymmetrical sharpening are two such heuristics (*Figure 1D*). As more processing

connotes a greater attentional demand (Johnston & Heinz, 1978), it would be favorable to employ this heuristic only when advantageous.

Previous work (Yu & Geng, 2019) has shown that shifting of the target template representation is a means of increasing target-distractor distinctiveness. Specifically, only when the target was linearly separable from the distractors did the target representation shift away from distractor values. This shifting in response to stimuli defined by a single feature dimension occurred to a similar magnitude regardless of degree of target-distractor similarity.

However, real-world target objects typically have multiple feature dimensions. Multidimensional stimuli are encoded differently than unidimensional ones (Lau et al., 2020; Dugué et al., 2017; Farashahi et al., 2020). This is likely related to the binding problem (Li et al., 2022), wherein it is unclear how the brain integrates individual features into bound multi-feature objects (see Zhang et al (2020) for recent neuroimaging evidence). Attention flexibly utilizes the informativeness of each dimension to select the target based on how target-distractor discriminability is best harnessed (Lee & Geng, 2019). Becker, Atalla, and Folk (2019)'s recent work to understand the nature of relational search when objects are defined in multiple dimensions implies that each dimension is perceived in isolation, such that each dimension of a bound object can adhere to a separate search heuristic. It is then under question how informativeness of search contributes to ease of search in each dimension while making target recognitions, given the distractor context.



<u>Figure 1:</u> Schema of target-distractor linear separability and similarity. A) Stimulus set where target (T) is separated from distractors (Ds) by a linear function ("linearly separable" or "unilateral distractors relative to the target"). B) Stimulus set where target (T) is separated from distractors (Ds) by a nonlinear function ("not linearly separable" or "bilateral distractors relative to the target"). C) Effect of target-distractor linear separability on target representation in memory. Adapted from Yu & Geng (2019). D) Schematic of target-distractor similarity. E) Hypothesized degree of target template representation shifting in memory.

The present study aims to further investigate the role of relative dimension informativeness on perceptions of target-distractor distinctiveness. In these experiments of interleaved twodimensional visual search and one-dimensional probe trials, we hold distractor features in one dimension linearly separable from and highly similar to distractors. This design induces shifting to compensate for difficult discriminability in that dimension (Yu & Geng, 2019). We then manipulate the second dimension which is not linearly separable from but differs in terms of perceptual similarity (low, high) to see how dissimilarity in this second dimension affects shifting in the first. If shifting behavior is automatic, it should be deployed whenever there is target-distractor linear separability.

However, we expect that shifting is adaptive and will only need to be utilized when target recognition is difficult. Specifically, there will need to be both linear separability between the target and distractors and a high level of target-distractor similarity in order to induce the shifting response. When there is low target-distractor similarity, this strategy will be unnecessary because this parameter already lends sufficient levels of target-distractor distinctiveness to make the

target recognition. The non-linearly separable dimension should not shift either, as shifting away from distractors on either side of the target would essentially "cancel" each other out.

In order to determine the role of the distractor context in multidimensional target search, the impact of the degree of target-distractor similarity and linear separability on target-distractor distinctiveness needs to be further understood. Given that different dimensions of feature conjunctions are represented independently (Becker et al., 2019), we expected that the dimensions' tuning curves would shift independently and according to both the degree of target-distractor similarity and linear separability properties of that dimension. If target-distractor similarity moderates the ability to make a target recognition, the relative ease of search at low target-distractor similarity should be reflected as a high search efficiency and a (relatively) veridical template representation. Shifting would not confer an additional advantage in making target-identifying judgments if the stimuli were already readily discriminable. When there is a high degree of ambiguity given high target-distractor similarity however, search should be inefficient and only the linearly separable dimension is expected to shift. This will elucidate whether this optimal representation is held through either an automatic or adaptive process.

To preview the results, linear separability of the target and distractors' feature values shift the target representations independently for each dimension, but this effect is moderated by the degree of target-distractor similarity and which dimension is linearly separable. This provides further evidence of the importance of how informative the distractor context is in making target selection and subsequent recognition judgments.

EXPERIMENT 1AB Method:

Participants Mirroring the sample sizes used in Yu & Geng (2019), we recruited 20 participants per condition. Seventy three University of California, Davis (UCD) undergraduate students participated for course credit after giving consent, in accordance with the UCD Institutional Review Board. Participants were randomly assigned to one of two conditions (high target-distractor similarity condition: 1A [11 females, 4 males, 2 non-binary people; median age = 20; 2 left-handed, 15 right-handed], 1B [13 females, 7 males, median age = 19; 20 right-handed]; low target-distractor similarity condition: 1A [9 females, 6 males, 1 non-binary person; median age = 20; 16 right-handed], 1B [13 females, 7 males, median age = 19, 20 right-handed]). All demographics were self-reported, where all had normal (or corrected-to-normal) visual acuity and color vision.

Apparatus The experiment was administered on a Dell desktop (monitor size: 27", resolution: 1080p (1920x1080)), assuming a viewer distance of 60 cm.

Stimuli The stimulus properties were independently manipulated between feature dimensions (*Figure 2*). Distractors were always linearly separable from the target in one dimension but not in the other dimension. The linearly separable dimension always had a high degree of target-distractor similarity, but the non-linearly separable dimension had either a high or low degree of target-distractor similarity.

The stimuli were Shape-Color conjunctions created from two radially organized stimulus spaces. Colors were taken from a CIELAB isoluminant color space (Bae et al., 2015). Shapes were selected from the Validated Circular Shapes dataset (VCS; Li et al., 2019). Color and shape were integrated via MATLAB 2021a at the time of data collection

The specific distractor values chosen were based on an independent just-noticeable difference (JND) task (see *Just-noticeable difference task section of Supplementary Information*) that equated discriminability and standardized the cognitive distance of distractors from the target between the color and shape spaces. Given pilot data (*see Main task section of Supplementary Information; Figures S2-8*) where the majority of participants discriminated between the stimuli with performance approaching ceiling, the JND was adapted such that its value was 5 degrees in both the CIELAB and the VCS space. Distractor objects were created by combining each Color with a Shape of a corresponding unit multiplier (u) from the target. For example, a distractor 2 JND units away from the target (u = 2) was 5*2 = 10 degrees away in both feature spaces.



<u>Figure 2:</u> Stimuli and design of Experiment 1. A single condition in which Shape distractors are linearly separable and Color distractors are not linearly separable (Experiment 1A) is shown. A) Illustration of the visual search Shape-Color pairings of distractors relative to the target. Red lines connect possible feature pairs in the high target-distractor similarity condition; orange lines connect possible pairs in the low target-distractor similarity condition; the gray line depicts target features in both conditions. B) Sample of trials in Experiment 1A's target-distractor similarity condition. C) The same as (B), except color is unilateral and shape is not (Experiment 1B).

The linearly separable dimension always had high target-distractor similarity (u: + [1, 2, 3]), whereas the non-linearly separable dimension set included values with either high (u: +/- [1, 2, 3]) or low (u: +/- [6, 7, 8]) target-distractor similarity. Two color and shape targets were selected (u: 0) – one target combined shape 84 with Color R.G.B 210.151.216 and the other was shape 264 and R.G.B 58.190.179. These target features were chosen because they had previously been shown to be centers of categories wide enough for shifting behavior to be detected (Yu & Geng, 2019; *unpublished data*). Inscribed within these objects were either right- or left-leaning lines (+/- 45 clockwise degrees off of a vertical line), respectively.

The questionnaire was a series of the following questions:

- 1. How successful do you think you were at pinpointing the target shape in the wheel task?
- 2. How hard did you try to pinpoint the target shape in the wheel task?
- 3. How successful do you think you were at pinpointing the target Color in the wheel task?
- 4. How hard did you try to pinpoint the target Color in the wheel task?
- 5. In what order did you use Color and shape to find the target during the search task?
- 6. How successful do you think you were at finding the target in the search task?

- 7. How hard did you try to find the target in the search task?
- 8. How focused were you over the course of this experiment?

Experimental Design and Procedure Participants responded to stimuli presented in two interleaved tasks, a visual search task (360 trials) and a memory probe task (120 trials).

Visual search arrays had a set size of 4 but the search task was a 2-alternative forced choice task, where participants made either a left mouse click indicating that the inscribed line was left-leaning or a right mouse click if the line was right leaning. Though this left some ambiguity as to which stimulus was being recognized as the target within a trial, participants' recognition accuracy was made clear across trials. Feedback was delivered via an audible tone (high frequency for a correct target recognition and low frequency for an incorrect target recognition).

The memory probe results were obtained through either a Shape or Color wheel with 6 unidimensional reference points positioned on the periphery of the circle. Participants moved the mouse cursor over the circumference of the circle, which centrally enlarged a stimulus corresponding to that position in the feature dimension's circular space. As participants were instructed to prioritize precision, they made a left mouse click once they found a Shape or Color stimulus matching the remembered target feature.

Other than question 5 (1: 'shape first', 2: 'Color first', 3: 'both at the same time'), all questions asked participants to rate different processing aspects of the visual search and probe tasks on a scale of 1: 'not at all' to 9: 'very much'.

Data Cleaning Participants with mean visual search accuracies below 75% were excluded. Search trials with reaction times between 250 ms and 5000 ms were included (removing outliers in the upper quartile given the reaction times' interquartile range) as were probe wheel responses within +/- 60 degrees of the target. This resulted in the inclusion of 92.5% and 95.8% (1A) and 95.7% and 99.6% (1B) of trials of the high and low target-distractor similarity conditions, respectively, visual search trials. We included 100% and 100% (1A) and 99.2% and 99.9% (1B) of memory probe trials of the high and low target-distractor similarity conditions, respectively, in subsequent analyses.

Statistical Analysis The designs for each target set were counterbalanced between individuals within a similarity condition in order to ensure that the results were not an artifact of the selection of specific feature values. Two-sample *t*-tests were used to compare behavior between target-distractor similarity groups. Effect size (Cohen's *d*) was calculated by finding the difference between the distributions in response to target-distractor similarity and linear separability.

In the case when the response distributions compared were of unequal variances, we tested the distribution differences through the Welch's t-test; Student's t-test was used otherwise. To determine how veridical the mean target representation was, we performed one sample *t* tests relative to a mean of 0. We compared inverted encoding scores (reaction time/ accuracy) as they related to mean target representation veridicality as an indicator of how efficiency relates to target shifting. Two-way ANOVA tests were run to determine how shifting behavior related to processing efficiency using the Python package 'statsmodels'.

To determine the effect of linear separability and target-distractor similarity in each dimension, the probability of target 'yes' response was determined for each probe by similarity condition. The main analysis consisted of modeling the probability of "target yes" responses to each probe Color and shape with a Gaussian distribution. We computed . 99a Bayes Factor (BF) which denotes the likelihood that the alternative hypothesis will be supported in comparison to the null hypothesis given the data using the R package 'BayesFactor'.

Maximum likelihood (ML) estimation was used to calculate best fitting parameters of the Gaussian distribution. We used the R package maxLik to maximize the model's likelihood function given the data (Henningsen & Toomet, 2011; Lagarias et al., 1998; Dempster et al., 1977). This estimation was performed separately for each participant, where traditional statistical tests were then run on the resulting ML parameters to examine differences by condition.

EXPERIMENT 1A Results and Preliminary Discussion:

In this experiment, the target Shape was always linearly separable and very similar (high targetdistractor similarity) to distractor objects in this dimension. The target Color was always nonlinearly separable from distractor Colors, but had either high or low target-distractor similarity.



<u>Figure 3:</u> Visual search performance in Experiment 1A. When there was low Color target-distractor similarity, participants were A) more accurate and B) faster in selecting and identifying the target.

When only the Shape dimension was linearly separable, low Color target-distractor similarity resulted in an advantage in accuracy (*Figure 3A*: $\mu_{high} = 0.92$, $\mu_{low} = 0.99$, 95% *CI_{high}* [0.88, 0.96], 95% *CI_{low}* [0.98, 0.99], Welch's t(106.61) = -7.37, p < 0.001, d = 1.01, $BF_{10} > 1000$) and reaction time (*Figure 3B*: $\mu_{high} = 1436.85$, $\mu_{low} = 893.40$, 95% *CI_{high}* [1315.67, 1558.02], 95% *CI_{low}* [813.06, 973.75], Student's t(196) = 14.87, p < 0.001, d = 2.11, $BF_{10} > 1000$). This strong dissociation likely reflects how strongly the Color dimension's informational content guides search (Bramão et al., 2011).



<u>Figure 4:</u> Target representation veridicality. A) When Shape was linearly separable, neither Color nor Shape shifted away from distractors in either target-distractor similarity condition. B) Violin plots confirmed the veridical nature of the remembered representations.

To examine whether this efficiency in visual search was associated with a change in the target template representation in memory, we next looked at the memory probes (*Figure 4*). The non-linearly separable Color ($\mu_{high} = 3.18$, t(16) = 0.94, p = 0.36; $\mu_{low} = 1.43$, t(15) = 1.06, p = 0.30; $BF_{01} = 0.47$) and linearly separable Shape dimensions remained largely veridical ($\mu_{high} = -1.28$; t(16) = -0.94, p = 0.36; $\mu_{low} = -0.71$, t(15) = -0.96, p = 0.35; $BF_{01} = 0.35$) regardless of target-
distractor similarity condition. This lack of repulsive shifting, even slightly shifting *towards* distractors was surprising.



<u>Figure 5:</u> Behavior on visual search and memory tasks. Inverted encoding scores (reaction time/ accuracy) were A) bigger at high target-distractor similarity than B) at low target-distractor similarity.

Given the differences in processing search efficiency (*Figure 3*) and the lack of shifting behavior in response to distractor context properties (*Figure 4*), we then investigated these components in tandem as an indication of how this search heuristic is related to search behavior (*Figure 5*). Participants who negatively shifted their mean target representations away from positive, linearly separable distractors also performed search more efficiently. As efficiency was higher at low target-distractor similarity overall ($\mu_{negative} = 863.88$, $\mu_{positive} = 936.12$) than at high targetdistractor similarity ($\mu_{negative} = 1535.47$, $\mu_{positive} = 1676.26$), there was a significant difference in processing efficiency between direction shifted (F(1) = 0.16, p < 0.001). Within similarity conditions, there was not an advantage from negatively shifting the target representation away from positive distractors (t(15) = -0.92, p = 0.37). These results suggest that the heuristics employed during visual search interplay with biases in memory to facilitate efficient target recognition.



<u>Figure 6:</u> Self-reported reliance metrics. At high target-distractor similarity in Color and linear separability in the shape dimension, participants showed a bias towards relying upon Shape to make a target recognition. At low target-distractor similarity in color and linear separability in the shape dimension, participants show a preference for using color to make the target recognition.

When Shape was linearly separable, participants reported some notable trends, which were largely similar between target-distractor similarity conditions (*Figure 6*). Participants were more confident in locating the Shape probe ($\mu_{high} = 7.47$, $\mu_{low} = 7.44$) than the Color probe ($\mu_{high} = 5.94$, $\mu_{low} = 6.75$; t(32) = 3.93, p < 0.001), as unambiguous Shape target-distractor linear separability likely facilitated discriminability. High target-distractor similarity required participants to devote marginally more effort to do the search task compared to at low target-distractor similarity (*shape*,

color: $\mu_{high} = 6.06, 6.76; \mu_{low} = 5.50, 5.81$), where they also felt more confident ($\mu_{high} = 7.88, \mu_{low} = 8.06$) and found it easier ($\mu_{high} = 5.65, \mu_{low} = 4.69$) to recognize the target in the low similarity condition.

Given that participants had a higher central tendency at low than at high target-distractor similarity ($\mu_{high} = 1.47$, $\mu_{low} = 2.19$), participants capitalized on the stark Color differences to guide initial search; at high target-distractor similarity though, individual differences dictated participants' dimension preference, using either Color or Shape between participants. During visual search, participants in the low target-distractor similarity condition were marginally more confident ($\mu_{high} = 7.88$, $\mu_{low} = 8.06$, t(32) = -0.53, p = 0.59) and needed to devote less effort ($\mu_{high} = 5.65$, $\mu_{low} = 4.69$; t(32) = 0.91, p = 0.37) to make the target recognition.

EXPERIMENT 1B Results and Preliminary Discussion:

In this experiment, the target Color was always linearly separable and very similar (high targetdistractor similarity) to distractor objects in this dimension. The target Shape was always nonlinearly separable from distractor Shape, but had either high or low target-distractor similarity.



<u>Figure 7:</u> Visual search performance. When there was low Color target-distractor similarity, participants were A) more accurate, but B) not quicker in making the target recognition.

When only Color was linearly separable, low Shape target-distractor similarity resulted in an advantage in accuracy (*Figure 7A:* $\mu_{high} = 0.90$, $\mu_{low} = 0.98$, 95% *CI_{high}* [0.86, 0.93], 95%*CI_{low}* [0.97, 0.99], *Welch's* t(106.61) = -8.26, p < 0.0001, d = 1.07, *BF*₁₀ > 1000) but not reaction time (*Figure 7B:* $\mu_{high} = 1176.15$, $\mu_{low} = 1176.32$, 95% *CI_{high}* [1037.48, 1314.81], 95%*CI_{low}* [1070.24, 1282.40], *Student's* t(238) = -0.04 * 10^-1, p = 0.997, $d = 0.05 * 10^-2$, *BF*₀₁ = 0.14). This lack of dissociation according to Shape target-distractor similarity may reflect how Shape is not a perceptually uniform feature dimension (Li et al., 2019); with an irregular representation in cognitive space, response rates may also reflect ambiguity.



<u>Figure 8:</u> Target representation veridicality. A) When Color was linearly separable and had high target-distractor similarity, this feature dimension shifted to an off-veridical value, as was confirmed by (B).

Here, the linearly separable Color dimension at high target-distractor Shape similarity shifted away from distractors the most out of all other target-distractor similarity and linear separability pairings (*Figure 8A*). Specifically, Color negatively shifted more at high target-distractor similarity than at low target-distractor similarity (*Figure 8B*; $\mu_{high} = -4.09$, t(19) = -3.44, p < 0.01; $\mu_{low} = -$ 2.27, t(18) = -2.60, p < 0.05; $BF_{01} = 0.56$). Shape did not need to shift at either target-distractor similarity level, as there was already sufficient target-distractor distinctiveness conferred in the system (through featural distinctiveness at low similarity and through relational distinctiveness at high similarity, *Figure 9C;* $\mu_{high} = 1.07$, t(18) = 1.39, p = 0.18; $\mu_{low} = 1.64$; t(19) = 3.01, p < 0.01).



<u>Figure 9:</u> Performance efficiency by template shifting between visual search and memory probe tasks did not significantly differ between target-distractor similarity conditions.

Now that the processing efficiency diverged in accuracy but not reaction time (*Figure 7*) but the association between target-distractor linear separability and similarity as it relates to target shifting in memory appears tenuous (*Figure 8*), we next looked at how these two behaviors were related (*Figure 9*). As in Experiment 1A, low target-distractor similarity ($\mu_{negative} = 1214.44$, $\mu_{positive} = 1199.72$) evoked marginally greater efficiency than high target-distractor similarity ($\mu_{negative} = 1267.54$, $\mu_{positive} = 1349.47$). This ultimately did not produce a difference by similarity condition and direction of shifting (*F(1) = 0.24*, *p = 0.63*). So although a negative shift was associated with higher target recognition accuracy, this did not translate into greater efficiency overall in making the target recognition.



<u>Figure 10:</u> Self-reported reliance metrics for Experiment 1B. Subjective ratings ranged from 1 = ""not at all' to 9: "very much" for all questions except for #5 (1: 'shape first', 2: 'Color first', 3: 'both at the same time').

Reliance trends were comparably reflective when Shape instead was linearly separable (*Figure 10*). Participants were marginally more confident in locating the Shape probe ($\mu_{high} = 7.00$, $\mu_{low} = 7.16$) than the Color probe ($\mu_{high} = 6.47$, $\mu_{low} = 6.68$). This is particularly surprising as it was expected that confidence would always be higher in the linearly separable dimension with perhaps a stronger Color effect given its reliable informational content (Bramão et al., 2011). High target-distractor similarity required participants to devote more effort to do the search task compared to at low target-distractor similarity (*Shape, Color:* $\mu_{high} = 6.80$, 7.47; $\mu_{low} = 5.79$, 7.16), where

they also felt more confident ($\mu_{high} = 7.60$, $\mu_{low} = 8.32$) and found it easier to identify the target in the low similarity condition.

Given that the central tendency at low target-distractor similarity was lower than at high targetdistractor similarity ($\mu_{high} = 1.80$, $\mu_{low} = 2.11$), this suggests that when featural distinctiveness is high, search is guided by the linearly separable dimension; when featural distinctiveness is low, individual preferences dictated which single feature dimension that they would use as a guide.

At low target-distractor similarity, participants were more confident in their success during visual search ($\mu_{high} = 7.60$, $\mu_{low} = 8.32$), which translated into less effortful search ($\mu_{high} = 8.20$, $\mu_{low} = 6.16$). With the strong Color dimension being linear separable, these markers of search processing bore starker differences between target-distractor similarity conditions relative to when Shape was linearly separable.

GENERAL DISCUSSION:

These results expand previous research by examining how multidimensional target objects are represented in memory given the distractor context. We show that target-distractor similarity and linear separability interact such that the mean target representation shifts away from distractors in order to imbue optimal target-distractor distinctiveness when adopting that heuristic is advantageous (Johnston & Heinz, 1978). This effect was dimension-specific though, as this memory bias depended upon which dimension the bias could be expressed in.

Though the present work is limited in scope such that interpretations of broad mechanisms may not be appropriate, the present work aligns with and diverges from past work (Yu & Geng, 2019) in some notable ways. While there are only two levels to the target-distractor similarity by targetdistractor linear separability designs presented here (Experiment 1A: Shape is unilateral, Experiment 1B: Color is unilateral), these results also show that target shifting is not a binary process. As seen in Experiment 1B, intermediate levels of template representation shifting occur even in sub-optimal conditions. This may reflect differences in ability to extract information across feature dimensions. Though this was not explicitly studied, visual inspection of response distributions appear to show signs of asymmetrical sharpening against linearly separable distractors (*Figure S9*).

Whereas the work of Becker and colleagues (2010, 2020) created tension with the feature similarity gain model (Martinez-Trujillo & Treue, 2004), this work and other studies by the present authors (Geng et al., 2017; Yu & Geng, 2019) further undercovers how target-distractor distinctiveness affects the dynamics of object search to show that these mechanisms interact. Target-distractor linear separability produces relational informational content, while target-distractor similarity imbues featural informational content. Depending on the properties of the stimulus context, these levers are adaptively pressed to facilitate object recognition.

This tension was previously relaxed when studies found a synthesis between the relational and optimal accounts of target search (Hamblin-Frohman & Becker, 2020; Yu & Geng, 2020). Specifically, it was found that search was initially guided using a relational heuristic, with an object recognition decision using an optimal heuristic. The present work contributes that these adaptations based on target-distractor linear separability and similarity are responded to in a

manner that dissociates feature dimensions of multidimensional objects. Search was initially guided by the non-linearly separable dimension at low target-distractor similarity, while which dimension was used at high target-distractor similarity was subject to individual differences.

The informational content imbued among stimulus properties varies. As predictability of feature values informs search efficiency through assigning different levels of attentional priority (Witkowski & Geng, 2022), other factors such as prior knowledge, spatial relations, and naturalness of feature combinations also contribute to search dynamics (Guo et al., 2020; Bainbridge et al., 2019; Bramão et al., 2011). Among visual properties, different characteristics imbue different information to facilitate search in different ways (Stuart et al., 2020).

Different feature dimensions are known to inhabit cognitive spaces differently. Shape and Color, for example, have long been known to contribute to search differently (Olds et al., 2009). Though we attempted to place the studied dimensions on the same plane, their spatial regularities likely still did not align. Further, the computed just-noticeable difference metrics were insufficient when translated from the pilot to the main task (*Figure S1; unpublished data*), prompting the change to a smaller discrimination constant. While the large parameter may have been the result of methodological error in the just-noticeable difference task design or analysis, the difference between the tasks may reflect differences in responding to unidimensional versus multidimensional stimuli (Bahle et al., 2020).

This work suggests that there may be a "tradeoff" in conscious and subconscious responses to the distractor context. As Witkowski & Geng (2019) postulated that the target template may be biased in memory, "sacrificing" veridicality for a distinctiveness advantage, implicit shifting

behavior that reflected such a bias was simultaneously met with an explicit report of perceived accuracy. This may imply that this adaptive heuristic is not consciously made, but is a response to the stimulus context relative to the remembered template.

It is often posited that such an effect is not the result of a manipulation of memory, but is rather the result of perceptual processing as per the simultaneous contrast effect (Ratnasingam & Anderson, 2017). Recent work has refuted this claim though (Hamblin-Frohman & Becker, 2020), where making the target recognition with distractors present did not present a precision advantage; this study did not find a shifting effect however, this is likely the result of the distractors being well outside the window that produces this behavior (Scolari & Serences, 2009).

As mentioned above, we included only two levels of target-distractor similarity by target-distractor linear separability designs such that it is premature to ascertain whether one of these properties trumps the other when searching for a target. While self-report poses well-known issues, this work provides some interesting insights. Participants explicitly used the most informative dimension when completing the task, but this seemed to be subliminally related to shifting behavior.

However, these results are based on an incomplete dataset. While two target sets were delivered to counterbalance the presented stimuli and average across stimulus-specific idiosyncrasies, the final dataset was imbalanced such that the results may still reflect irregularities of the sampled stimulus spaces. Pilot data did not reveal such effects though. Even after model fitting once, some parameters (especially those describing metrics at high target-distractor similarity) had large variances that may suggest poor fit through the maximum likelihood estimation. Future work on

a full dataset should examine whether shifting behavior predicts processing efficiency as a stronger marker of how adaptive the shifting behavior is for facilitating target search. Studies using eyetracking methods would be useful in further clarifying search dynamics, especially for multidimensional objects.

In conclusion, featural distinctiveness relayed through target-distractor similarity and relational distinctiveness imbued through target-distractor linear separability interact to modulate target search efficiency. These factors are related to biases in memory that exaggerate visual differences to facilitate target recognition. Informational content of stimulus properties informs explicit search behavior, though this may not align with the employment of implicit heuristics. This work contributes to a growing body of research investigating how the distractor context is utilized to ensure efficient target search.

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Supplementary Information:

Just-noticeable difference (JND) task In order to simultaneously compare how independent dimensions are affected by linear separability and target-distractor similarity manipulations without regard to the specific dimensions used, the color and shape spaces used here need to be normalized in space. Differences in responses to different feature dimensions have been previously reported (Rutishauser & Koch, 2007; Olds et al., 2009; Lee & Geng, 2019). It is necessary to investigate how these dimensions are represented in perceptual space, as understanding the properties of these component parts informs the representation of the integrated object (Wolfe et al., 1989). Though these circular stimulus spaces have been shown to be perceptually uniform (Li et al., 2019; Bae et al., 2015), they likely do not occupy the same amount of cognitive space. The color and shape circular spaces likely do not have the same radii, such that the widths between contiguous stimuli are not equally discriminable. First making this determination assures that the stimuli are sufficiently distinct from each other (Yu & Grauman, 2015; York & Becker, 2020).

Participants Thirty-four participants were in each dimension group (color: 23 females, median age = 19; shape: 23 females, median age = 19.5). Participants gave informed consent and received course credit upon completion of the experiment, in accordance with the UC Davis

Institutional Review Board. Participants had normal or corrected-to-normal vision, including color vision.

Stimuli Continuous shape (Validated Circular Shapes dataset; Li et al., 2019) and isoluminant color (CIELAB; Bae et al., 2015) spaces were sampled from. The space around each target feature was bilaterally sampled (+/- [3, 6, 9, 12] degrees) in their respective feature spaces.

Design and Procedure Using the method of constant stimuli, participants were presented with unidimensional color patches and shape outlines. One dimension of the target stimulus and one other similar, bilaterally sampled probe of the same dimension were presented along the horizontal meridian, with a task to determine whether the two probes were identical or not. The target was presented with itself two times more often than all other pairings.

Analysis The probability of the 'same' response was computed for each difference in distance from target to the target probe. To reflect the inherent differences between the color and shape dimensions (task difficulty, primacy), the JND for each dimension was separately calculated by interpolating the average JND metric of the 70% and 30% response rates. This method both more fully captures the variable pattern at larger differences and also takes into account the similar response at smaller ones; this is reflected by the similar lapsing rates (denoted by the lower asymptotes indicative of the stimuli being readily discriminated) and different guessing rates (denoted by the upper asymptotes indicative of the stimuli not being readily discriminated) of the distributions between dimensions (Treutwein & Strasburger, 1999).

Results This revealed average JNDs of 5.91 and 8.30 for color and shape, respectively (*Figure S1*). This larger shape spread suggests that the shape dimension is less discriminable overall, such that even pairs with larger differences are perceived as the same, relative to the color dimension. So though the feature spaces are perceptually uniform and have a constant change in angular distance from target, these differential distributions can be interpreted as the radius of the circular shape space being larger than that of color, resulting in a greater cognitive distance between contiguous stimuli.



<u>Figure S1:</u> Results from the just-noticeable difference task. Participants were able to discriminate between colors around 6 degrees apart and shapes about 8 degrees apart.

EXPERIMENT S1AB:

EXPERIMENT S1AB Method:

Participants An à priori power analysis was conducted via the G*Power Suite on previously collected pilot data that compared two independently sampled means (*alpha* = 0.05, *power* = 0.95, *effect size* = 0.84). This resulted in a sample size of 34 per group, counterbalanced across two stimulus sets per each of two target-distractor similarity conditions (see *Stimuli* section below). One hundred thirty six University of California, Davis (UCD) undergraduate students participated for course credit after giving consent, in accordance with the UCD Institutional Review Board. Participants were randomly assigned to one of two conditions (high target-distractor similarity condition: S1A [25 females, 9 males, median age = 20], S1B [26 females, 7 males, 1 non-binary, median age = 19]), where gender identities were self-reported. All had self-reported normal (or corrected-to-normal) visual acuity and color vision.

Apparatus The experiment was administered online via Testable.org (<u>https://www.testable.org/</u>). To maximize consistent display properties across participants, the displays were calibrated to have the same visual angle, assuming a viewer distance of 60 cm.

Stimuli The stimuli were shape-color conjunctions created from two validated stimulus spaces. Colors were taken from a CIELAB isoluminant color space (Bae et al., 2015). Shapes were selected from the Validated Circular Shapes dataset (VCS; Li et al., 2019). Color and shape were integrated using Inkscape software (<u>https://inkscape.org/</u>). Two color and shape targets were selected – one target combined shape 264 with color R.G.B 58.190.179 and the other with shape 121 and color 210.151.216. These target features were chosen because they had previously been shown

to be centers of categories wide enough for shifting behavior to be detected (Bae et al., 2015; Yu & Geng, 2019; *unpublished data*).

Visual search displays were composed of one target and three distractors. For the sake of clarity, we will discuss this design in the context of Experiment S1A exclusively (Shape was the linearly separable dimension and Color was the non-linearly separable dimension), but these dimension-linear separability pairings were actually counterbalanced (Experiment S1A vs S1B).

Each dimension had the following properties (*Figure S2A*). The Shape distractor values were always highly similar to and linearly separable from the target value (u: + [1, 2, 3]). The Shape dimension was thus never informative in target-distractor featural distinctiveness, but always in target-distractor relational distinctiveness. The level of target-distractor similarity varied in the Color dimension. In the high similarity group (Shape_{high}/Color_{high}), the Color distractor values were also highly similar to but were not linearly separable from the target (u: +/- [1, 2, 3]). For the low similarity group (Shape_{high}/Color distractors were highly dissimilar to and not linearly separable from the target (u: +/- [1, 2, 3]). For the low similarity group (Shape_{high}/Color_{low}), Color distractors were highly dissimilar to and not linearly separable from the target (u: +/- [6, 7, 8]). This ensured that the distractors were sufficiently distant from the target, without hitting the ceiling of 90 degrees from the target that renders the task trivially simple (Scolari & Serences, 2009). This method manipulates the degree of target-distractor similarity constant. The Color dimension was then informative by target-distractor featural distinctiveness only in the low similarity condition, but never in target-distractor relational distinctiveness.

Memory probe displays showed single dimension target features sampling both sides of the target (u: +/- [1, 2, 3, 5]) in each of the Color and Shape dimensions (*Figure S2B*). The wide range of

probe stimuli ensured that the representation tuning curve could be seen in its entirety, as it was expected that participant responses would be maximally centered at (veridical target representation) or near (shifted representation) and then abruptly drop off.

The additional questionnaire contained the following:

- How much did you rely on the object's shape to identify the target? 1 = not at all, 9 = a lot
- How much did you rely on the object's color to identify the target? 1 = not at all, 9 = a lot
- 3. When did you use color and shape to identify the target? 1 = shape first, 2 = color first,
 3 = both at the same time
- 4. How focused on this experiment were you? 1 = not at all, 9 = very

Experimental Design and Procedure Participants were instructed on response parameters for the 4-alternative forced choice 4-(AFC) search and 2-AFC probe tasks, as well as to return gaze to central fixation between trials. Participants encoded the practice target stimulus for a self-paced duration and then completed a set of practice visual search and memory probe trials. The practice stimulus set's distractor feature values were not linearly separable from the target in either dimension so as not to bias expectations in the main task.



<u>Figure S2</u>: Stimuli and design of Experiment S1. A single condition in which shape distractors are linearly separable and color distractors are not linearly separable (Experiment S1A) with target 121-210.151.216 is shown. A) Illustration of the visual search shape-color pairings of distractors relative to the target. Red lines connect possible feature pairs in the high target-distractor similarity condition; orange lines connect possible pairs in the low target-distractor similarity condition; the gray line depicts target features in both conditions. B) Sample of trials in each of Experiment S1A's target-distractor similarity conditions, where visual search trials were randomly interleaved with memory probe trials after encoding the experiment target where shape is unilateral and color is not. C) The same as B, except color is unilateral and shape is not.

Participants then encoded the main study's target for a self-paced duration. After completing a series of visual search training trials to strengthen the target representation in memory, participants saw randomly interleaved visual search and probe trials (144 and 72 trials, respectively; *Figure S2C, D*). Search displays were composed of the target and three heterogeneous distractors placed on the vertices of an imaginary square around the display center. The search array was presented until a response occurred or 1500 ms elapsed. The response was a 4AF choice indicating the number displayed within the target object (1-4; "u": 1, "i": 2, "o": 3, "p": 4). The location of the four numbers, as well as the locations of the target and distractors, were randomly presented on each trial. The probe task was to indicate whether the unidimensional stimulus matched the target feature or not. All stimuli were presented over a dark gray background (hex #808080). Each participant completed the tasks with the same target stimulus for the entirety of the experiment.

Individual features were paired orthogonally across feature dimensions such that the stimulus set combined all sampled features; however, search arrays were designed to display each feature once within a trial without replacement. Although the colors of the visual search distractors were sampled from either side of the target overall, they were only sampled from one direction (positive or negative, relative to the target) on any given trial. This was done to standardize the local variability in features across arrays. The direction of color distractors was random, such that half of arrays had distractor features that deviated from the target in the positive direction of the positive direction and the other half deviated in the negative direction. Thus, the array could contain the following Shape/ Color *u* pairings in the Shape_{high}/Color_{low} condition: 0/0 (target), +1/-7, +2/-8, +3/-6.

The search trials were followed by 300 ms of visual feedback ("correct"/ "incorrect") after a response was made or 1500 ms had elapsed. This was followed by an inter-trial interval of 1000 ms, during which time participants were instructed to return their gaze to the fixation cross at the display center. Probes of target features were sampled with four times the frequency of all other probes so as to ensure sufficient power for further analyses, with a "u" response indicating that the probe matched the remembered target feature and "i" indicating that it did not. In one of the stimulus sets, the u = -2 stimulus erroneously had the u = -3 feature, so that u = -3 was presented twice as frequently as it was supposed to. This is not expected to have a significant effect, as the stimulus sets were counterbalanced between. After all search and probe trials were completed, participants were shown two screens asking for ordinal (1-9) measures of self-reported reliance on each dimension when making the target recognition and level of attentiveness throughout the experiment.

Statistical Analysis For each probe, we computed the proportion of "target 'yes'" clicks. Because the response for each probe in our probe task is independent, the probabilities of responding "yes" to all the probes do not sum to 1. We therefore introduced a subject-specific scaling parameter *a* that scales the distribution from each subject. An individual who has a small value of *a* is more conservative in responding "yes"; conversely, an individual who has a large value of *a* is more liberal in responding "yes".

Porwal and Raftery (2022) advocate for the use of Bayesian modeling as a valid method of hypothesis testing to predict the posterior probability distribution. All parameters were estimated using a hierarchical Bayesian analysis (HBA) parameter estimation method. To perform HBA, we used the R package Bayesian Regression Models using 'Stan' (brms; Bürkner, 2017, 2018).

Normal and Gamma distributions were used to set the hyper priors of the normal mean ($\mu \sim$ Normal (0, 1)), standard distance factor from target ($\sigma \sim$ Gamma (5, 1)) and free parameter ($a \sim$ Normal (1, 1)). Given the small number of data points per participant, we only estimated the group parameter values to capture commonalities across individuals. Each chain was run with 5000 samples, with the first 2500 warm-up samples discarded as burn-in. A total of 4 chains were run. Convergence was assessed by computing the Gelman-Rubin \hat{R} statistic for each parameter. The range of \hat{R} values across all group parameter estimates were between 0.99-1.10, suggesting satisfactory convergence. Goodness of fit was visually inspected with the posterior predictive check method. The p value that is reported is the probability that the distribution's mean is less than 0, where a large p corresponds to a large shift for that distribution away from 0 as a metric for target representation shifting.

Learning over the course of the visual search component of the main task was assessed. The percent accuracy on each trial of the visual search task was tracked by averaging across all participants within a similarity condition. These averages were then aligned over the course of all the trials and were then fitted by non-linear regression fit functions separately for each similarity condition.



EXPERIMENT S1A Results and Preliminary Discussion:

<u>Figure S3:</u> Experiment S1A (Shape is linearly separable and has high target-distractor similarity) visual search performance differs by target-distractor similarity. Maroon violin plots depict the Shape_{high}/Color_{high} condition, while goldenrod plots depict Shape_{high}/Color_{low}. Results show that A) mean accuracy in target recognition is higher at low target-distractor similarity and that B) mean response time is lower at low target-distractor similarity. C) Effect of learning on target search.

Red lines indicate performance in the high target-distractor similarity condition and the orange line shows the low-similarity condition.

Analysis of visual search performance During the visual search task, the low target-distractor similarity groups performed better overall. In Experiment S1A (Shape is linearly separable), processing efficiency was higher at low target-distractor similarity: accuracy, *Figure 4A*: $\mu_{high} = 0.89$, $\mu_{low} = 0.95$, 95% *CI_{high}* [0.85, 0.92], 95%*CI_{low}* [0.93, 0.97], t(66) = -3.58, p = 0.001, d = -0.87, BF₁₀ = 45.10; response time, *Figure 4B*: $\mu_{high} = 1503.36$, $\mu_{low} = 1016.24$, 95%*CI_{high}* [1432.35, 1574.36], 95%*CI_{low}* [952.52, 1079.96], t(66) = 10.01, p < 0.001, d = 2.58, BF₁₀ > 1000). This was expected because the low target-distractor similarity of the features in the non-linearly separable dimension allowed the target to be easily discriminated on that dimension. Both groups were able to effectively complete the task, despite its increased difficulty in the high similarity condition (as reflected in the larger mean response time).

In addition to low target-distractor similarity being associated with a faster, more accurate target recognition, participants in this condition also learned to represent the target accurately more quickly than when there was high target-distractor similarity. Though both conditions had the same distractor-distractor similarity widths, the featural target-distractor distinctiveness facilitates target search perhaps by exaggerating target-distractor distinctions.



Figure S4: Group averages of target "yes" responses. Solid curved lines are Gaussian distribution fits. All error bars are the 95% confidence intervals. A) The high similarity group in Experiment S1A. When there was high target-distractor similarity, the unilateral dimension shifted away from the visual search distractors. B) The low similarity group in Experiment S1A. At low targetdistractor similarity, the unilateral dimension did not shift. Model predictions for posterior distributions for each dimension. Probability density functions of the distributions' means by target-distractor similarity group and dimension are shown. Left column shows the predicted mean distributions of the Color and Shape dimensions when Shape has high target-distractor similarity, right column shows the predicted mean distributions of the Color and Shape dimensions when Shape has low target-distractor similarity.

Analysis of memory probe trial responses It was then in question whether this difference at encoding was reflected in how veridically the target was represented in memory (Lilburn et al., 2019). Several insights could be gained through visual inspection. In the high similarity condition (*Figure S4A*), the linearly separable Shape dimension shifted farther away from the positively sampled distractors than the non-linearly separable Color dimension. In the low similarity condition (*Figure S4B*), both the linearly separable and the non-linearly separable dimensions shifted away from the distractors to a similar extent. This co-shifting is evidence that the low target-distractor similarity in the non-linearly separable dimension was sufficiently diagnostic of the target such that its representation did not need to shift and compensate for its target-distractor similarity in order to maintain a high level of target search efficiency.

These biases in target recognition were confirmed through plotting the predicted central tendencies of the response distributions for each similarity condition, separated by dimension (*Figure S4C, D*). The linearly separable dimension ($\mu_{Shape} = -0.39$, $\sigma_{Shape} = 1.36$, $p_{Shape} = 1.00$) shifted more than the non-linearly separable dimension ($\mu_{Color} = -0.03$, $\sigma_{Color} = 1.55$, $p_{Shape} = 0.99$) dimension in the high similarity condition. In the low similarity condition, the linearly separable ($\mu_{Shape} = -0.31$, $\sigma_{Shape} = 1.70$, $p_{Shape} = 1.00$) and the non-linearly separable ($\mu_{Color} = -0.12$, $\sigma_{Color} = 1.80$, $p_{Color} = 1.00$) dimensions shifted to a similar intermediate degree. Thus, when target-distractor similarity did not confer distinctiveness, it was advantageous to hold that dimension in memory as an optimal, off-veridical template. This was not necessary when there was relatively high distinctiveness. While it is outside the scope of this paper to discuss the dynamics between these two feature dimensions, it is not surprising that the two behave differently (Lee & Geng, 2019).



<u>Figure S5:</u> Self-reported reliance metrics. A) When both feature dimensions had high targetdistractor similarity, participants showed a bias towards relying upon the linearly separable Shape dimension to make a target recognition. B) When Color had low target-distractor similarity, participants showed a preference for using this dimension to make the target recognition.

Dimension reliance Individual differences likely play a significant role in how veridically each dimension of the target is represented (Lafer-Sousa et al., 2015). How much participants relied on each dimension depended on which of the two dimensions was linear separable and the level of target-distractor similarity. When both dimensions had high target-distractor similarity (*Figure S5A*), participants relied on the linearly separable Shape dimension more ($\mu_{Shape} = 7.44$, $\mu_{Color} = 5.35$, 95%CI_{Shape} [6.81, 8.07], 95%CI_{Color} [4.41, 6.30], t(33)_{Color-Shape} = -3.16, p < 0.01, d = -0.54, BF₁₀ = 10.95). While it was expected that this condition would reflect participants' inherent biases in using one dimension over the other, this result is surprising in that Color is usually the preferred diagnostic dimension relative to Shape; this suggests a primacy in responding according to target-distractor similarity though (*Figure S5B*), participants relied much more heavily on that dimension ($\mu_{Shape} = 4.12$, $\mu_{Color} = 8.21$, 95%CI_{Shape} [3.08, 5.15], 95%CI_{Color} [7.65, 8.76], t(33) = 5.99, p < 0.0001, d = 1.03, BF₁₀ > 1000). So though the non-linearly separable dimension was not informative by linear separability relative to the target, it was still relied upon because it was

informative in terms of target-distractor similarity. Thus, the mode of informativeness of a dimension exerts a strong influence on which visual properties were used in order to identify a target.

It is then in question whether these results were the result of domain-specific processing. We thus replicated Experiment S1A with a counterbalanced feature dimension and linear separability design.



EXPERIMENT S1B Results and Preliminary Discussion:

<u>Figure S6:</u> Experiment S1B visual search performance differs by target-distractor similarity. Error bars reflect the 95% confidence interval on the mean accuracy and response time in each condition. A) Mean accuracy in target recognition is higher at low target-distractor similarity. B) Mean response time is lower at low target-distractor similarity. C) Learning trajectories by target-

distractor similarity condition, given accuracy of visual search performance in Experiment S1B. Maroon denotes high target-distractor similarity in the Color dimension, whereas goldenrod depicts low target-distractor similarity.

Analysis of visual search trials Processing efficiency when Color was linearly separable produced the following results. There was not an accuracy advantage from low target-distractor similarity in the shape dimension (*Figure S6A*: $\mu_{high} = 0.90$, $\mu_{low} = 0.96$, 95% *CI_{high}* [0.87, 0.92], 95%*CI_{low}* [0.94, 0.97], t(66) = -4.94, p < 0.001, d = -1.18, BF₁₀ > 1000). Compared to Experiment 1A where instead Color had either high or low target-distractor similarity, this suggests a possible interaction between this property and which feature dimension it is affecting. However, this condition did show an advantage in response time to select and identify the target (*Figure S6B*: $\mu_{high} = 1409.11$, $\mu_{low} = 1186.26$, 95%*CI_{high}* [1313.4, 1504.78], 95%*CI_{low}* [1124.21, 1248.30], t(66) = 3.76, p < 0.001, d = 0.99, BF₁₀ = 72.28). Target recognition could more readily be done when it was relatively easy to discriminate between the target and its distractors, than when they were less discriminable.

Given this variable effect on process efficiency during target search, results of this experiment showed that participants quickly learn the visual search task (Figure S7). Although accuracy at both similarity conditions approached ceiling, the low target-distractor similarity group learned faster. Increased featural target-distractor distinctiveness allows the task to be discriminated.



<u>Figure S7:</u> Group averages of target "yes" responses. Solid curved lines are Gaussian distribution fits. All error bars are the 95% confidence intervals. A) The high similarity group in Experiment S1B. When there was high target-distractor similarity, the unilateral dimension shifted away from the visual search distractors. B) The low similarity group in Experiment S1B. At low targetdistractor similarity, the unilateral dimension did not shift. Model predictions for posterior distributions for each dimension. Probability density functions of the distributions' means by target-distractor similarity group and dimension are shown. Left column shows the predicted mean distributions of the Color and Shape dimensions when Shape has high target-distractor similarity, right column shows the predicted mean distributions of the Color and Shape dimensions when Shape has low target-distractor similarity.

Analysis of memory probe trials Target feature recognition results for Experiment 1 also mirrored those of Experiment 1. The representation of the linearly separable dimension shifted away from distractors more than the non-linearly separable dimension when there was high target-distractor similarity (*Figure S7A, C*), but not when there was low target-distractor similarity (*Figure S7A, C*), but not when there was low target-distractor similarity (*Figure S7A, C*), but not when there was low target-distractor similarity condition. The non-linearly separable dimension shifted to a similar extent regardless of similarity condition. This highlights that the shifting strategy is used only when other methods of imbuing target-distractor distinctiveness are not present.

The predicted posterior distributions largely mirrored those of Experiment S1A (*Figure S7C, D*). The linearly separable dimension ($\mu_{Color} = -0.67$, $\sigma_{Color} = 1.14$, $p_{Color} = 0.64$) shifted more than the non-linearly separable dimension ($\mu_{Shape} = -0.18$, $\sigma_{Shape} = 1.56$, $p_{Color} = 1.00$) dimension in the high similarity condition. In the low similarity condition, the linearly separable ($\mu_{Color} = -0.27$, $\sigma_{Color} = 1.42$, $p_{Color} = 0.88$) and the non-linearly separable ($\mu_{Shape} = -0.28$, $\sigma_{Shape} = 2.04$, $p_{Shape} = 1.00$) dimensions still shifted to a similar intermediate degree. This lack of dissociation in the low target-distractor condition contradicts the hypothesis, in that even eliminating the predictability between distractor features did not prompt the two dimensions to be represented independently.

Analysis of self-reported reliance scores Which dimension was relied on was noisier now that the distractor dimensions were not associated (*Figure S8*). Both the linearly separable ($\mu_{Color} = 7.44$) and the non-linearly separable ($\mu_{Shape} = 6.38$) dimension were relied upon at high target-distractor similarity ($95\%CI_{Color}$ [6.83, 8.06], $95\%CI_{Shape}$ [5.41, 7.35], t(33) = 1.55, p = 0.13, d = 0.46). At low target-distractor similarity, participants again showed a marked preference for relying upon that dimension ($\mu_{Color} = 3.765$, $\mu_{Shape} = 8.41$, $95\%CI_{Color}$ [2.97, 4.56], $95\%CI_{Shape}$ [7.84, 8.98], t(33) = 8.69, p < 0.001, d = -2.38).



<u>Figure S8:</u> Self-reported reliance metrics. At high target-distractor similarity, participants did not show a bias in which dimension they relied upon to make a target recognition. At low targetdistractor similarity, participants showed a strong preference for relying upon the dimension that has low target-distractor similarity.

Taken together, the results provide evidence that the relational and featural distinctiveness imbued through the target-distractor linear separability and similarity, respectively, of the distractor context interactively modulate the degree to which adaptive shifting needs to be employed in order to more readily discriminate the target item from simultaneously presented non-targets. These two target-distractor properties independently moderated shifting behavior, thereby conferring separable modes to provide target-distractor distinctiveness. These results partially confirmed the hypothesis by showing that whichever dimension more easily facilitated target recognition was harnessed and that shifting occurred only when ambiguous featural distinctiveness made target recognition difficult.

Experiment S1 revealed several preliminary insights, namely that participants' behavior differed along with the joint design of the target-distractor properties here studied. Featural and relational distinctiveness moderate how the two dimensions defining a target are held in memory and
subsequently used to guide search. Metrics like search accuracy and reaction time revealed a dimension-specific effect, where target recognition behavior varied by mode of presentation.

Limitations to Experiment S1AB:

This research design held many drawbacks to be improved upon. Presenting the probes in a randomized serial visual presentation was incredibly time inefficient, leading to severe underpowering of the experiment; given that these experiments were administered online, we were under a strict time constraint to increase the likelihood that participants remained engaged with the tasks for the duration of the experiment.



<u>Figure S9:</u> Biases in memory by stimulus dimension in A) Experiment 1A and B) Experiment 1B. By visual inspection, responses to memory probes were relatively normally distributed such that

asymmetrical sharpening of the target representation against linearly separable distractors is not apparent.

Chapter 3:

Effectiveness of established and experimental interventions for pediatric ADHD: a scoping review

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Abstract:

Attention deficit/ hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders affecting American children. Established treatments have shown moderate levels of effectiveness, but experimental methods need to be integrated into treatment plans in order to advance treatment efficacies. In this scoping review sourcing literature from Google Scholar and PubMed and following PRISMA guidelines, we discuss the advantages and disadvantages of the broad range of interventions used to treat or evaluate pediatric ADHD and identify gaps in the literature.

Introduction

Attention deficit/ hyperactivity disorder (ADHD) is one of the most common

neurodevelopmental disorders worldwide, affecting around 8.7 - 9.8% of American children (Schnorrbusch et al., 2020; Bitsko et al., 2022). While symptoms of the disorder often persist into adulthood (Sibley et al., 2016), they can be readily seen in the behaviors of children and adolescents (hereafter referred to as "children") who tend to have outcomes like poor educational achievement, socializing abilities and overall health-related quality-of-life (Calub et al., 2019; Powell et al., 2021; Rushton et al., 2019; Wanni Arachchige Dona et al., 2023). These factors motivate the need to provide practical interventions that have significant impacts on both trained and untrained tasks. This would allow development of effective behavioral therapies that meaningfully alleviate this disorder's adverse symptoms translated from structured (e.g. laboratory, clinic) to unstructured (e.g. school) settings to improve the functional outcomes of this sizable patient population (Corrigan et al., 2023).

The ADHD behavioral profile is complex and heterogeneous (Luo et al., 2019; Mueller et al., 2017), where symptoms range in presentation and severity across patients. Patients exhibit a marked deficit in prolonged attention and response inhibition abilities (Breitling-Ziegler et al., 2020), exhibiting elevated rates of omission and commission errors that indicate respondents' level of inattentiveness and impulsivity respectively (Mühlberger et al., 2016). The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; Krull, 2022) outlines three sub-types: predominantly hyperactive/ impulsive (~4-11%), predominantly inattentive (~27-31%) and a combination of the two (~58-68%; Mattingly et al., 2012; Mauri et al., 2020). Differences in response inhibition and sustained attention are thought to rely on related but distinct substrates within this network, where there are behavioral and neural differences between ADHD subtypes (Hwang et al., 2019; Park et al., 2015).

These primary atypicalities integrate into secondary ones. Possibly resulting from poor working memory abilities (Fosco et al., 2020), patients need a higher level of stimulation than their typically developing peers to perceive stimuli (Li et al., 2022; Hong et al., 2021). Children with ADHD are prone to distraction, where this proneness for distractor-driven attentional capture is thought to be linked to patients' atypical eye and head movements though the causal directionality is unclear (Siqueiros Sanchez et al., 2020); this does not seem to affect their overall information processing abilities (Mangalmurti et al., 2020; Cho et al., 2022). Though these patients seem to exhibit intact feature search (visual search based on one feature; Mullane & Klein, 2008; Allen & Pammer, 2015), their search for feature conjunctions is impaired (visual search based on multiple features; Mason et al., 2003; Mullane & Klein, 2008); these abilities are indicative of information processing abilities in the domains of selective attention and working memory capacities (Hitch et al., 2020). Despite seemingly typical anatomy of peripheral visual structures (Bellato et al., 2022), children with ADHD exhibit atypical visual processing possibly as a compensatory mechanism associated with atypical neural signatures and functional connectivity differences in the frontoparietal network and associated cortices that are typically relied upon for this ability (Luo et al., 2021; Kumar et al., 2022).

Patients with ADHD have a marked lack of motivation to engage in certain goal-oriented tasks (Morsink et al., 2020; van der Oord & Tripp, 2020). This led Wasserman and Wasserman (2015) to stress that ADHD may be better characterized as a deficit in motivating efficient goal-directed attention allocation rather than a deficit in attention capacity itself. The symptomatology of this disorder is often viewed through the lens of a deficit model, though they are also associated with potential benefits (e.g. justice sensitivity, creativity and entrepreneurial mindset; Schäfer &

Kraneburg, 2012; Antshel, 2018). For the purposes of this review, we will primarily use the deficit perspective as a starting point to develop potentially effective therapeutics targeting ADHD's unfavorable outcomes. Given the broad range of atypical behavioral patterns exhibited, interventions for pediatric ADHD span a wide range of techniques that each have their own unique advantages and disadvantages. While multimodal interventions have been shown to be more effective than unimodal ones (Garcia Pimenta et al., 2021; Ou et al, 2020; but see Zhang et al., 2023a), we will constrain this review to the latter approach in order to examine baseline effects of these complementary interventions and allow for clearer comparisons to be drawn between them (*Box 1*).

- <u>Neuropharmacology</u>: non-supplement Western medication (stimulant or non-stimulant)
 <u>Behavioral training</u>:
 - <u>Psychosocial</u>: psychological training gained through e.g. meeting with a psychologist or introspection
 - <u>Psychophysical</u>: computerized perceptual training of tasks like visual search that do not use an avatar
 - Physical activity: exercise at various levels of intensity (low, moderate, high)
- <u>Digital health:</u> training delivered through the use of e.g. mobile applications, virtual meeting platforms

- Neuromodulatory training: direct or indirect non-invasive neural stimulation

- Virtual reality:
 - <u>Non-immersive</u>: computerized training with a task objective to navigate on-screen avatar
 - <u>Semi-immersive:</u> computerized training passively interacted with as user enters virtual environment from the avatar's perspective seen through a headset
 - Fully immersive: same as semi-immersive, except hand controller allows active interaction with virtual environment
- <u>Augmented reality:</u> user interacts with virtual elements situated in the real-world environment through the use of applications, etc.

Box 1: Overview of established and experimental interventions commonly used to

address symptoms of pediatric ADHD.

Some of these established and experimental intervention techniques may evoke a direct physiological effect while others can be considered as an indirect method of delivery. We will focus this review on monotherapies as a means for comparing the interventions at a unitary level; though interventions that integrate multiple techniques (e.g. virtual reality possibly including psychophysical and physical activity components), are still considered monotherapies because the patient encounters it simultaneously (Krzystanek et al., 2021). Given that they all have their own unique advantages and disadvantages when applied to the treatment of pediatric ADHD, we aim to shed light on how effective and practical each is to inform whether they are good candidates for being integrated into treatment plans. Our objectives for this scoping review are thus fourfold:

- Survey the literature for effect sizes of each method, as a marker of how well each intervention works compared to a control group or groups.
- 2. Survey the literature for each intervention's ability to evoke either the near or far transfer effect, as a marker for how its outcomes generalize to untrained tasks.
- 3. Survey the literature for reported cost-effectiveness of each method, as a marker of how economical it is for practitioners to employ the intervention.
- 4. Survey the literature for reported risk of side effects of each method, as a marker of how safe the intervention is for patients.

Method of scoping review

A wide range of interventions for pediatric ADHD are here reviewed; we specified search terms and labels given common descriptive words used in the relevant literature (*Figure 1*). To examine how the general advantages and disadvantages outlined above contribute to each intervention's effectiveness on a practical level, we examined each method from different perspectives to gain a holistic understanding of how these interventions can be utilized to produce the optimal results for this patient population. There are several factors by which pediatric ADHD treatments can be compared that are integral in determining how effective it is to incorporate into a treatment regimen. Though there are countless factors that inform the efficacy of an intervention, we here operationalize it as a combination of study effect sizes, reported ability to evoke the near and far transfer effects, reported cost-effectiveness and reported risk of side effects. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews guidelines (<u>http://www.prisma-statement.org/Extensions/ScopingReviews</u>) because this format reflects this multi-pronged approach on a sparse literature base.

| | | Quantitative | Qualitative | | | |
|--------|---|---|---|---------------------------|------------------------------------|--|
| | Factors | Effect Size | Transfer Effect | Side Effects | Cost- effectiveness | |
| | Search term | "effect size" Hedges | "transfer effect" OR "untrained task" OR reading OR math* | "side effect" OR safe* | cost OR *expensive -valuable | |
| | Neuropharmacology | medication OR of | drug OR pharm* | | | |
| | Behavioral training (psychosocial) | psychoeducation OR "talk therapy" OR psychotherapy OR CBT OR counseling | | | | |
| | Behavioral training (psychophysical) | "computer training" OR computerized OR psychophysic* | | | | |
| รเ | Behavioral training (physical) | exercise OR exergam* OR physical | | | | |
| ntior | Behavioral training (digital health) | "digital health" OR "mobile health" OR telemedicine OR telehealth | | | | |
| Iterve | Neuromodulatory training | neurofeedback OR tDCS OR TMS OR EEG OR MEG | | | | |
| l | Virtual reality (non-immersive) | "non-immersive" "virtual reality" | | | | |
| | Virtual reality (semi-immersive) | "semi-immersive" OR classroom "virtual reality" | | | | |
| | Virtual reality (fully immersive) | "immersive" "virtual reality" | | | | |
| | Augmented reality | "augmented reality" | | | | |

<u>Figure 1.</u> Search terms by intervention and factor for conducting the present scoping review. The base search query on Google Scholar was "children adolescents intitle:adhd OR intitle:"attention deficit" intitle:meta OR intitle:systematic" with the addition of the intervention phrase and factor, as the question dictated.

Eligibility criteria In short, we reviewed various previously described secondary analyses (systematic reviews and meta-analyses only) published on PubMed and Google Scholar that summarized randomized controlled trials (RCTs) examining intervention outcomes for children with clinically diagnosed ADHD relative to each factor discussed. Though symptoms change over

patients' lifespans, it is highly likely that symptoms persist from childhood to adolescence (Shaw & Sudre, 2020; Owens et al., 2015). In line with the relevant literature, we will here group them together since they share functional similarities in their daily lives (e.g. attending grade school, etc.).

The search was constrained to articles published between January 2019 and July 2023 to account for the rapid rate of technological advances that these interventions enjoy. We included secondary analyses published in peer-reviewed journals written in English, separately for each of the included factors (*Figure 1*). When secondary analyses drew from primary articles spanning a range of ages and neuropsychiatric disorders, we selectively included papers evaluating children with ADHD. Papers were excluded if the interventions targeted caregivers (e.g. parents and teachers) of children with ADHD rather than the children themselves, if the paper included the search term only to say that it fell within the source paper's exclusion criteria, if the qualitatively assessed factors' search term appeared in the paper without providing an evaluation on it, if the paper only reviewed adults, or if only within-intervention category comparisons were made (e.g. efficacy of psychostimulants versus non-stimulants, without a baseline control).

In accord with our eligibility criteria, screening articles involved excluding them if they exclusively drew from papers that studied adult patients with ADHD, if they explicitly stated that the searched for term is irrelevant to their work, or if the qualitatively assessed factors' search term appeared in the paper without providing an evaluation on it. Though there are known gender differences in ADHD behavioral expression (Loyer Carbonneau et al., 2021), we did not group by this factor in and of itself since we were interested in effects on gender-agnostic applications (e.g. school).

Factors The present review sought to extend Dijk and colleagues' (2021) review of the costeffectiveness of established pediatric ADHD interventions, investigating more factors relevant to treatment efficacy and surveying a broader range of intervention methods. We describe each intervention's effectiveness in relation to four properties. 1) A common comparison metric is effect size between patients' performance on a behavioral task, pre- and post- intervention, relative to age-matched controls. We limited the search to secondary analyses that explicitly used the Hedges' q statistic to account for the small sample size of primary articles they drew from. This statistic can be interpreted using the same convention as used with Cohen's d(0.2): small effect size, 0.5: medium effect size, 0.8: large effect size). 2) We qualitatively examined the ability of the intervention to evoke a transfer effect. For example, if the experimental task was to respond to a continuous performance task (CPT) in a semi-immersive virtual classroom, a near transfer effect would be evident if the behavioral profile was the same when doing the CPT in a real classroom; a far transfer effect would be if the CPT improved academic outcomes like reading proficiency. 3) We then examined reported costs of intervention development and administration regardless of insurance on a qualitative level. Cost-effectiveness is measured by incremental costeffectiveness ratios using metrics like the quality adjusted life-year (QALY), which measures the price of an intervention over the period of a year relative to treatment as usual. 4) Reported severity of side effects likewise reflects the reported adverse outcomes that arise from use of the treatment method.

Analysis of factors After noting the total number of secondary analyses using each intervention (*Table 1*), papers' full texts were skimmed and further analyzed by the first author (RAR) for their factor-relevant content (*Tables 2 - 5*). Duplicates were only removed at this final step, unlike the

screening and eligibility stages typically employed. Though some secondary analyses sourced a mixture of articles of child and adult ADHD patients, articles were selected to ensure that evidence from only children and adolescents were included in the present review. We standardized the reported effect sizes so that positive values indicated that the intervention was favored to the control. When articles reported multiple effect sizes (e.g. separating by predominant symptoms; Bemanilzadeh et al., 2021) we reported the range of values within each study. We further reported the range of effect sizes across studies within an intervention method.

Results and Preliminary discussion of scoping review

Through an exclusion process (*Table 1*), we ultimately included 66 unique secondary articles (meta-analyses, systematic reviews) that met the inclusion criteria. To reflect the sparseness of the literature's information on these topics, we compiled frequency-of-reporting metrics of included articles to focus future research. See *Tables 2-5* to review each source of included evidence along with the evidence it provides.

<u>Table 1:</u> Estimated counts of secondary analyses describing each intervention's relationship to the factors discussed here from January 2019 to July 2023. Counts are presented as a number sequence, where the first number denotes how many reviews were identified as eligible during the search period for that intervention overall, the second number denotes how many of these reviews mentioned each factor and the third number denotes the number of reviews with substantial

information (i.e. provided an evaluation of that factor's relation to the intervention).

| | | Quantitative | Qualitative | | |
|--------|---|--------------|-----------------|--------------|------------------------|
| | Factors | Effect Size | Transfer Effect | Side Effects | Cost- effectiveness |
| | Neuropharmacology | 826 128 2 | 826 252 2 | 826 32 0 | 826 172 12 |
| | Behavioral training (psychosocial) | 417 91 4 | 417 172 0 | 417 22 5 | 417 97 0 |
| | Behavioral training (psychophysical) | 455 112 2 | 455 193 2 | 455 20 1 | 455 104 2 |
| รเ | Behavioral training (physical) | 584 119 8 | 584 224 0 | 584 28 3 | 584 125 2 |
| ntior | Behavioral training (digital health) | 97 18 2 | 97 33 0 | 97 3 0 | 97 20 2 |
| Iterve | Neuromodulatory training | 389 91 6 | 389 152 0 | 389 17 2 | 389 79 8 |
| IJ | Virtual reality (non-immersive) | 110 | 100 | 100 | 111 |
| | Virtual reality (semi-immersive) | 25 9 4 | 25 10 0 | 25 1 0 | 25 9 2 |
| | Virtual reality (fully immersive) | 420 | 410 | 400 | 432 |
| | Augmented reality | 530 | 530 | 500 | 520 |

| Intervention | Source Paper | Sub-Paper | Reported Effect Sizes |
|---------------------|--------------------------|------------------------|--|
| | Idrees et al., 2023 | Brams et al., 2017 | 0.44, 0.19, 0.45 |
| | | Findling et al., 2005 | -0.07, 0.13, 0.13, -0.11, 0.11, 0.02, 0.03, 0.25, 0.32, -0.14, 0.18, 0.05, 0.02, 0.19, 0.12, 0.11, 0.16, 0.22, 0.12, -0.19, -0.02, 0.20, -0.12, -0.09, 0.16, -0.05, 0.03 |
| Neuropharmacology | | Findling et al., 2011 | 0.37, 0.25, 0.39, -0.30, -0.21, -0.05, -0.11, -0.01, 0.37 |
| | | Mattingly et al., 2019 | 0.40, 0.40, 0.13 |
| | | Tannock et al., 1995 | 0.02, 0.85, 0.38, 0.20, 1.01, 0.86 |
| | | Wigal et al., 2009 | -0.12 |
| | Chiu et al., 2023 | | 0.62, 0.66 |
| | Xue et al., 2019 | | 0.68, 0.83 |
| Behavioral training | Iznardo et al., 2020 | | 0.36 |
| (psychosocial) | Zhang et al., 2023 | | 0.12, 0.25, 0.41 |
| | Fabiano et al., 2021 | | 0.66, 0.72 |
| | Parsons et al., 2019 | Parsons et al., 2007 | 0.92 |
| | | Adams et al., 2009 | 0.55 |
| | | Pollak et al., 2009 | 0.94 |
| Behavioral training | | Pollak et al., 2010 | -0.29 |
| (psychophysical) | | Bioulac et al., 2012 | 0.85 |
| | | Negut et al., 2016 | 0.81 |
| | | Areces et al., 2018 | 0.13 |
| | Westwood et al., 2023 | | 0.24, 0.24, 0.32, 0.26 |
| | Chueh et al., 2022 | | 0.32, 0.25 |
| | Varigonda et al., 2021 | | 0.38, 0.35, 0.39 |
| | Sun et al., 2023 | | 0.97 |
| Behavioral training | Bustamante et al., 2022 | | 0.42, 0.50, 0.41, 0.30 |
| (embodied) | Qiu et al., 2023 | | 0.90, 1.38 |
| | Seiffer et al., 2022 | | 0.33 |
| | Vysniauske et al., 2020 | | 0.63 |
| | Kleeren et al., 2023 | | 1.46 |
| | Phillips et al., 2020 | Corkum et al., 2016 | 0.17, 0.49, 0.16, 0.19 |
| | | Hiscock et al., 2015 | 0.33, 0.03, -0.17 |
| Behavioral training | Bemalizadeh et al., 2021 | Beck et al., 2010 | 0.33 |
| (digital health) | | Chacko et al., 2008 | 0.02 |
| | | Klingberg et al., 2005 | 0.20 |
| | | Myers et al., 2015 | 0.41 |

| | Lee et al., 2022 | | 0.65, 0.2, 0.87 |
|------------------------------------|---------------------------|-------------------------------|------------------------------------|
| | Chiu et al., 2022 | | 0.32 |
| | Riesco-Matías et al., | | 0.33, 0.25, 0.17, 0.16 |
| | Westwood et al., 2021 | Breitling et al., 2016 | 0.77, 0.66 |
| | | Munz et al., 2015 | 0.38, -0.36, 0 |
| Neuromodulatory | | Prehn-Kristensen et al., 2014 | -0.57 |
| training | | Soff et al., 2017 | 0.11, 0.3 |
| | | Soltaninejad et al., 2019 | -0.02, 0.33, 0.27 |
| | | Nejati et al., 2017 | 0.09, 1.43, 0.42, 1.36, 0.47, 0.37 |
| | | Sotnikova et al., 2017 | -0.43, 0.01, 0.08 |
| | Chung et al., 2022 | | 0.26, 0.24, 0.16, 0.17, 0.26, 0.22 |
| | Qiu et al., 2023 | | 0.70 |
| Virtual reality (non-immersive) | | | N/A |
| | Corrigan et al., 2023 | Bioulac et al., 2020 | 0.40 |
| | | Kim et al., 2020 | 1.15 |
| | | Skalski et al., 2021 | 1.10 |
| Virtual reality | Roberts et al., 2021 | Clancy et al., 2006 | 0.09, 0.53, 0.09 |
| (semi-immersive) | | Nikolas et al., 2016 | 0.28, 0.19, 0.59 |
| | Romero-Ayuso et al., 2021 | Bioulac et al., 2020 | 0.64 |
| | Parsons et al., 2019 | | 1.18, 0.70, 0.45 |
| Virtual reality (fully immersive) | | | N/A |
| Augmented reality | | | N/A |

<u>Table 2:</u> Results of the "effect size" systematic search. The source paper is the secondary article that was output by the database search, the sub-paper was the primary article that the source paper reviewed, and the evidence was the reported Hedge's g effect size.

| Intervention | Source Paper | Reported Transfer Effect Evidence |
|---|--------------------------|--|
| Neuropharmacology | | N/A |
| Behavioral training (psychosocial) | | N/A |
| Behavioral training (psychophysical) | Westwood et al., 2023 | Positive effects seen on visuospatial and verbal WM performance did not transfer to other neuropsychological processes and/or academic outcomes and in some cases were no longer statistically significant when analyses were limited to trials with semi-active control arms. |
| | Stewart et al., 2019 | Although evidence is not fully developed for these practices, initial research demonstrates they hold promise for serving students with or at risk of ADHD. |
| Behavioral training (embodied) | | N/A |
| Behavioral training (digital health) | | N/A |
| Neuromodulatory training | | N/A |
| Virtual reality (non-immersive) | | N/A |
| Virtual reality (semi-immersive) | Corrigan et al., 2023 | Given the positive association between global cognitive functioning and academic performance (Tikhomirova et al. 2020), and social functioning (Bellanti and Bierman 2000), VR-based interventions may benefit the daily life of (children OR adolescents)with ADHD in terms of school performance and peer relations |
| Virtual reality (fully immersive) | | N/A |
| Augmented reality | | N/A |

<u>Table 3:</u> Results of the "transfer effect" systematic search. The source paper is the secondary article that was output by the database search, the sub-paper was the primary article that the source paper reviewed, and the evidence was the reported text in reference to the intervention's ability to produce either the near or far transfer effect.

| Intervention | Source Paper | Reported Cost-effectiveness Evidence |
|---|---------------------------------|---|
| Neuropharmacology | Sampaio et al., 2022 | Among pharmacotherapies for ADHD, different combinations of stimulant/non-stimulant medications for children were cost-effective at willingness-to-pay thresholds reported in the original papers |
| | Tourjman et al., 2022 | psychosocial interventions generally require an important investment in resources, both from the treated individuals (and their caregivers) and from the institutions offering the service. Such investment may be more costly for economically disadvantaged populations that, critically, appear to be at greater risk for ADHD |
| | Power et al., 2022 | It is also important to note that current methods of psychological and neuropsychological testing can be time consuming [43] and costly |
| | Payen et al., 2022 | the individualistic scope and often expensive nature of psychotherapy sessions |
| Behavioral training (psychosocial) | Vysniauske et al., 2020 | continuous and costly supervision from a behavioral therapist |
| Behavioral training (psychophysical) | Rodrigo-Yanguas et al., 2022 | Treatments for ADHD are usually costly in terms of time, energy, and economic resources for patients and families. This way, serious video games may serve as a complementary activity which may reduce those costs. |
| | Varigonda et al., 2020 | Exercise may be a potentially cost-effective and readily implementable intervention to improve executive function in these populations |
| Behavioral training (embodied) | Kotulska et al., 2023 | In comparison to drug therapy, physical activity is devoid of side effects and less expensive |
| | Vysniauske et al., 2020 | [physical exercise] does not require continuous and costly supervision from a behavioral therapist |
| Behavioral training (digital health) | Păsărelu et al., 2020 | Developments in mental health delivery (e.g., Internet-delivered therapy) have brought important advantages, such as access to treatment in remote areas, lower costs as compared to face-to-face treatment |
| Neuromodulatory training | Chiu et al., 2022 | There are also criticisms against [EEG-NF's] cost-effectiveness, time-consuming nature, and lack of long-lasting benefits |
| | Lin et al., 2022 | given the high cost of EEG-NF |

| Virtual reality (non-immersive) | | N/A |
|--------------------------------------|--------------------------|---|
| Virtual reality (semi-immersive) | | N/A |
| Virtual reality (fully immersive) | Corrigan et al., 2023 | Despite the existence of evidence-based treatments for ADHD, a high number of children do not have access to such interventions. Significant barriers in treatment access exist and are related to costs |
| Augmented reality | | N/A |

<u>Table 4:</u> Results of the "cost" systematic search. The source paper is the secondary article that was output by the database search, the sub-paper was the primary article that the source paper reviewed, and the evidence was the reported text on how cost-effective the intervention is for its usage by patients and their families.

| Intervention | Source Paper | Reported Side Effects Evidence |
|-------------------|------------------------|---|
| | Bryant et al., 2022 | For all the drugs currently licensed in the UK to treat ADHD in children and adolescents (methylphenidate, lisdexamfetamine, dexamfetamine, atomoxetine and guanfacine), the BNFC lists increase of anxiety and depression as common or very common side effects |
| | Pan et al., 2022 | headache is common in children with ADHD, both as part of the clinical presentation as such and as a side effect of some standard medications |
| | Pouchon et al., 2023 | [Methylphenidate] seems to be safe and efficient in the treatment of ADHD |
| | Wang et al., 2021 | In ADHD group, the side effect of decreased appetite showed the largest effect size |
| | Patra et al., 2019 | atomoxetine causes side effects like nausea, vomiting, decreased sleep, and decreased appetite |
| | Rodrigues et al., 2020 | Baseline documentation of vital signs and symptoms that can be exacerbated with ADHD medication treatment or experienced as side effects of treatment is critical for later evaluation of tolerability of a given medication, (i.e., sleep, appetite, presence of tics, psychosis, suicidality, mood dysregulation/irritability, blood pressure, heart rate, weight, height |
| Neuropharmacology | Carucci et al., 2021 | Long term MPH appears to be associated with a statistically significant impact on height and weight in ADHD children and adolescents |
| | Boland et al., 2020 | These findings emphasize the critical importance of stimulants on the prevention of [motor vehicle crashes] and support of safe driving in individuals with ADHD. |
| | Zhu et al., 2023 | A common side effect of methylphenidate, which is a commonly utilized stimulant drug, is appetite suppression, leading to reduced weight gain and decreased appetite in patients, which ultimately affects BMI and body size |
| | Chiu et al., 2023 | only the risk of poor appetite was higher in the psychostimulant group risks of irritability, sleep disturbance, prone to cry, and anxiety were slightly higher in preschool children receiving psychostimulant treatment than those treated with placebos |
| | Solmi et al., 2020 | on the basis of the available safety evidence: the preferred agents are likely to be methylphenidate among anti-ADHD medications |
| | Yu et al., 2023 | Guanfacine is safe and effective for treating ADHD |
| | Faraone et al., 2019 | Although fluoxetine is safe in children |
| | Zhu et al., 2023 | PRC-063 [an extended-release methylphenidate] is an efficacious and safe treatment for ADHD, especially in children and adolescents. |

| | - | |
|---|-------------------------------|--|
| | Rocha et al., 2023 | the use of [guanfacine] in children and adolescents for the treatment of ADHD symptoms has already been identified as safe and effective, presenting, like most adverse effects, mild to moderate phenomena |
| | Farhat et al., 2022 | medications are mostly safe and effective in reducing the severity of ADHD symptoms in the short term |
| | Ojinna et al., 2022 | treatment with [methylphenidate has] a good safety and tolerability profile |
| | Parkin et al., 2022 | using medication is safe and effective increases willingness to use medication |
| Neuropharmacology | Tourjman et al., 2022 | adverse effects such as reduced appetite, abdominal pain, reduced sleep, hypertension and headaches [68,69] may preclude the use of medication in some individuals. In children, stimulants can delay gains in height and weight |
| | Nageye Cortese et al., 2019 | [fasoracetam] [had] minimal [a]dverse effects reported among patients |
| | Sugaya et al., 2023 | stimulants are generally safe in the short-term for the treatment of preschoolers with ADHD |
| | Barranco-Ruiz et al., 2019 | pharmacotherapy has been related to side effects such as poor tolerance, no response to treatment, and even dependence |
| | Ching et al., 2019 | More carefully monitored studies are needed to investigate the efficacy, tolerability, and safety of methylphenidate titrated purely on clinical grounds without reference to any set maximum dose |
| | Hu et al., 2021 | it is clear that reboxetine and atomoxetine are safe |
| Behavioral training (psychosocial) | | N/A |
| | Chen et al., 2022 | [Computer-based] cognitive training is a non-invasive, safe, and inexpensive intervention that can be implemented quickly and conveniently in a home setting |
| Benavioral training (psychophysical) | Zulauf-McCurdy et al., 20 | Cognitive training['s a]dverse effects of cognitive training were compared with controls in 3 of 13 basic efficacy comparisons (23.1%)—none reported significant side effects relative to controls |
| Behavioral training | Huang et al., 2022 | Exercise intervention has been considered a potentially complementary approach for ADHD in recent years because it is safe |
| (embodied) | Barranco-Ruiz et al., 201 | the [mind-body therapies] could active the liberation of this hormone without the typical adverse side effect of these chemical medications |
| Behavioral training (digital health) | Păsărelu et al., 2020 | Developments in mental health delivery (e.g., Internet-delivered therapy) have brought important advantages, such as access to treatment in remote areas, lower costs as compared to face-to-face treatment |
| | Chen et al., 2022 | Even though people in some areas are quarantined at home because of the pandemic, in a way telemedicine can reduce concerns |

| | Brauer et al., 2021 | itching, tingling and headache revealing no significant effect |
|---------------------------------------|---------------------------|--|
| | Salehinejad et al., 2022 | tDCS was found safe with no reported serious side effects |
| | Salehinejad et al., 2020 | The safety of tDCS in adults [35] and children has been documented in previous studies [36] and confirmed by recent large dataset [37] although more evidence is needed for its safe application in pediatric populations |
| Neuromodulatory training | Westwood et al., 2020 | the most commonly reported side effects were mild tingling and itching [and headache] |
| , , , , , , , , , , , , , , , , , , , | Cosmo et al., 2020 | tDCS for ADHD appears safe |
| | Makkar et al., 2021 | non-invasive stimulation techniques [(e.g. rTMS and tDCS)] are well tolerated and safe for therapeutic use |
| | Yan et al., 2019 | neurofeedback (NF) has been proposed by a number of research groups as an effective and safe option for ADHD |
| | Zulauf-McCurdy et al., 20 | [tdcs is] without significant differences in adverse effects relative to placebo. |
| Virtual reality (non-immersive) | Corrigan et al., 2023 | VR is both feasible and safe |
| | Romero-Ayuso et al., 2021 | VR [is a] safe environment |
| Virtual reality (semi-immersive) | Corrigan et al., 2023 | Similar promising results concerning safety of immersive VR emerged, as there were no adverse effects |
| Virtual reality (fully | Romero-Ayuso et al., 2021 | VR [is a] safe environment |
| immersive) | Corrigan et al., 2023 | VR is both feasible and safe |
| Augmented reality | | N/A |

<u>Table 5:</u> Results of the "side effect" systematic search. The source paper is the secondary article that was output by the database search, the sub-paper was the primary article that the source paper reviewed, and the evidence was the reported text related to the safety of using the intervention.

Established interventions

Neuropharmacology Medications used to treat pediatric ADHD include stimulants (i.e. methylphenidate) and non-stimulants in isolation or in combination with other treatments. The

effect sizes computed through secondary articles of double-blinded RCTs comparing the efficacy of pharmacological agents vary widely, ranging from -0.12 to 1.01 (Idrees et al., 2022); this may be due to differences in sampled age ranges and/ or pharmacological agents used, as well as the diverse symptoms targeted (e.g. different markers of the autonomic nervous systems versus global ADHD symptoms, inattention or hyperimpulsivity; Chiu et al., 2023). Medications' estimated costs are generally cost-effective (Sampaio et al., 2021). Recent secondary analyses show that these medications are generally considered a safe treatment option (Chiu et al., 2023); they do carry a risk of incurring moderate levels of adverse side effects including headache, anxiety and depression, and a decreased appetite that may have further effects on children's heights and weights (Bryant et al., 2022; Pan et al., 2022; Tourjman et al., 2022). The ability for medication-use to elicit the far transfer effect trends positive; methylphenidate has shown to somewhat improve various ADHD symptoms (e.g. focus, impulsivity, working memory abilities, disruptive behavior) in both laboratory and naturalistic settings (Chan et al., 2023).

Pharmacological agents are powerful tools for treating ADHD in that their effects are continuous, not context-specific, for the duration that the drug is bioactive within the patients' bloodstreams but have negligible cognitive effects after treatment is discontinued (Tamminga et al., 2021; Faraone et al., 2023). Jang and colleagues (2021) showed that though methylphenidate is effective at decreasing perceptual processing speed, the drug must be paired with increased working memory demands in order to produce neural signatures that mimic those of their typically developing peers. These results suggest that neuropharmacological agents will exhibit favorable transfer effects; Pelham and colleagues (2022) found that methylphenidate usage was associated with a more typical behavioral profile in the classroom, yet patients did not learn the material better than their typically developing peers. Given that this stimulant medication has been shown

to have a positive effect on ADHD children's ability to ignore audiovisual distractors (Guo et al., 2023; Pelham Jr. et al., 2011; Pires et al., 2009), these altogether suggest that ADHD is more complex than a proneness to be distracted (Wasserman & Wasserman, 2015).

While medications are reported as being cost-effective (Dijk et al., 2021), this likely reflects that its immense costs of development are subsidized by health insurance so as not to be distributed to patients (Dalsgaard et al., 2014). Medications have a wide range of cost-effectiveness metrics for children (\$3,017/QALY to \$37,780/QALY (Sampaio et al., 2021). Extensive use of these medications may have a host of drawbacks though, where there is an unclear link to gastrointestinal distress (Young et al., 2021), cardiovascular distress (Liu et al., 2018) and delayed growth trajectories (Carucci et al., 2021); moreover, its use in certain subgroups may be unwise (Krinzinger et al., 2019). Further, patients' symptoms are often medication-resistant, have a variable degree of success at treating symptoms and are often not adhered to and may be otherwise abused (Khan & Aslani, 2020; Vertessen et al., 2021). Iterative dose titration poses a major disadvantage, as patients may suffer from administration of a suboptimal dosage for an extended period of time before an appropriate treatment plan is found (Erder et al., 2012). Given this uncertainty and lack of added benefit from medication use (Lambez et al., 2020), the predominantly employed liberal approach of medicating children as the first course of action upon diagnosis is especially concerning.

Behavioral training (psychosocial) Given that this second-line class of behavioral treatments (e.g. psychoeducation, psychotherapy) have a weak-to-moderate effect (effect sizes ranging from 0.12 to 0.83; Zhang et al., 2023b; Xue et al., 2019), this intervention may be best-suited for only a subset of the target population. Though it is unclear whether the immediate benefits gained from

cognitive training are generalizable to untrained tasks (0/417 articles), its use has shown a moderately small effect overall (Lee et al., 2022). There were no secondary articles on side effects within this reporting period. Its high cost overall suggests that psychosocial intervention may be a burdensome and inequitable path forward (Payen et al., 2022; Tourjman et al., 2022).

Cognitive training's individualized approach may have the requisite flexibility to address the wide variability of behavioral patterns expressed even within ADHD subtypes (Luo et al., 2019). While traditional psychotherapy often shows limited success for these patients, a psychodynamic approach focused on nurturing the mentalization capacities between the therapist, child, and caregivers (through fostering compassion for each other) may be an effective method to flexibly address the children's atypical behavioral patterns and provide patient support (Conway et al., 2019). Indeed, this approach may be preferable to pharmacological methods as an initial post-diagnosis intervention (Pelham & Altszuler, 2020; Coles et al., 2019), as its personalized and interactive aspects may facilitate retention of trained behaviors that ultimately translate into positive functional outcomes (Dvorsky et al., 2021).

As a method that works implicitly to modulate participants' cognitive states, psychotherapy's effectiveness is often muffled; though protocols are designed to measure such complex functions as attentiveness and executive functioning capacities, psychosocial cognitive training relies heavily on the sensitivity of the often insufficiently sensitive measures used to evaluate child ADHD (Schneider et al., 2019; Volz-Sidiropoulou et al., 2013). This class of interventions is generally less effective than other interventions (e.g., medication, neurofeedback training and psychoeducation, though this intervention used behavioral parent training; Roy et al., 2022). Though there are currently no secondary analyses examining psychosocial interventions' safety,

it is often assumed that its side effects upon administration are relatively negligible; a special report by Barkley (2018) disagrees, highlighting that this portrayal is largely due to insufficient reporting. This intervention is generally thought of as costly, as skilled practitioners' rates are steep. Tran and colleagues (2018) found that a Child Life and Attention Skills program, where caregivers and children collaboratively underwent psychosocial treatment, produced a \$3997 higher cost relative to treatment as usual; while other parent-focused treatment may be more cost-effective than this program, it is less costly than leaving the ADHD symptoms unresolved.

Experimental interventions

Behavioral training (psychophysical) This type of computerized training can be designed to address a wide variety of symptoms; for deficits in selective and sustained attention, patients can be given a visual search or CPT task, respectively. In the few studies investigating these factors, side effects and cost-efficiency of psychophysical training (computerized, avatar-less perceptual training) are relatively favorable (Rodrigo-Yanguas et al., 2022). Studies have shown a weak-to-moderate effect between condition groups on tasks ranging from verbal working memory up to reading comprehension though (-0.29 to 0.94; Parsons et al., 2019). It is not yet clear whether strong task generalizability effects can be gained through this method. While Stewart and colleagues (2019) posit that it does produce carryover effects, Westwood and colleagues (2023) did not see evidence of transfer from working memory training to other functional domains (i.e. academic performance).

Computerized training is likewise highly flexible, depending on the deficit being targeted. Children are inherently motivated to engage with the method, allowing them to complete the intervention

course in a relatively short amount of time (Rodrigo-Yanguas et al., 2022). Indeed, children with ADHD who undergo computerized eye tracking training improve their inhibitory gaze control abilities amid distractor interference; Lee et al., 2021). While Kassai and colleagues (2019) did find near transfer effects, they did not find strong evidence of a far transfer effect when training various executive functions (e.g. working memory, cognitive flexibility and inhibitory control).

While this treatment method's cost-effective nature and quantifiable outcomes are potentially more objective and enduring than self- or caregiver-report (Ambrosio et al., 2020; Pilling et al., 2020), it retains several disadvantages. Among the noise produced given that people with ADHD are known to exhibit altered perceptual abilities and that there is a high degree of intrinsic variability across patients (Fuermaier et al., 2017; Luo et al., 2019), it is yet unclear how meaningfully this intervention's signal will be able to be extracted. Moreover, children with ADHD (especially those with the predominantly inattentive and combined subtypes) are, by definition, characteristically inattentive; this poses a problem where patients' data are often underpowered due to an elevated rate of response omission (Witton et al., 2017).

Behavioral training (physical activity) Physical training (exercises ranging in intensity from yoga to distance running) has shown high cost-efficiency in children with ADHD (Varigonda et al., 2021; Li et al., 2023). Moderate-to-high effect sizes have been elicited with this technique compared to other interventions, where the literature shows a wide range of values (g = 0.01 to 1.46; Chueh et al., 2022; Kleeren et al., 2023). Side effects of moderate task-oriented exercise are generally sufficiently small for the activities thus far included such that this class of interventions is considered safe (Huang et al., 2022). Transfer effects have not been studied at the secondary level given the eligibility criteria.

The effect of exergaming has been studied as a means to target the mind-body connection as it relates to several skills implicated in childhood ADHD (e.g. or; Benzing & Schmidt, 2019; Nejati, 2021; Shema-Shiratzky et al., 2018). How effective physical training is at improving executive functioning is unclear (Cahill et al., 2019; García-Baos et al., 2019; Qiu et al., 2023), where outcomes are moderated by intensity of training (Varigonda et al., 2020; Tsai et al., 2021).

Research into this intervention's ability to produce the far transfer effect is ambiguous; As Seiffer and colleagues (2021) posited that physical activity training may have wider implications, Pontifex and colleagues (2013) showed that aerobic exercise improved children's overall cognitive and key academically-relevant abilities. However, this method may not be sufficiently engaging to prompt the patient to persist long enough to gain a therapeutic benefit (Dekkers et al., 2017). It is generally safe in moderation though (Huang et al., 2022), such that its high cost-effectiveness suggests that it may be a viable option for some patients (Wymbs et al., 2021).

Behavioral training (digital health) It is not yet clear how effective digital health interventions (e.g. mobile health applications reminding patients to engage in a behavior, telemedicine, etc.) as a group are for addressing ADHD children's symptoms, though studies tend to produce low-to-medium effect sizes (-0.17 to 0.49; Phillips et al., 2020). Though research into the safety of digital health is sparse, telemedicine has been a boon for delivering cognitive training for children with ADHD while maintaining safety (Chen et al., 2022). Its cost-efficiency to patients is seemingly high (Păsărelu et al., 2020). Further secondary research is needed to determine how generalizable digital health benefits are to untrained tasks, as well as what is the nature of side effects associated with it.

With a broad range of tools, this class of interventions has produced improvements in various domains (e.g. primary ADHD symptoms and cognitive function; Bemanalizadeh et al., 2021). Further, the flexibility that these tools afford gives them the advantage of conveniently and continuously collecting data and/ or delivering cues while patients engage in a task without being restricted to a clinical or laboratory setting as a means of increasing intervention efficiency. Though there is scant research on this topic, costs likely vary widely by tool based on their development and distribution processes.

Though this method of delivery allows for measures to be more readily taken, it also carries several disadvantages. Periodically cuing mobile health applications in particular runs the risk of diverting patients' often inherently compromised focus from goal-directed tasks (Tavakoulnia et al., 2019). These interventions carry high potential risks of breaches of confidentiality and hinders intervention standardization (Santosh et al., 2023), limiting its usefulness from both patients' and practitioners' perspectives.

Neuromodulatory training This umbrella term describes the class of non-invasive techniques that provide either perceptual or direct stimulation, using tools like electroencephalography or transcranial direct current stimulation. Effect sizes for neuromodulatory training range from very weak to moderate when comparing treatment groups (-0.57 to 1.43; Westwood et al., 2020), likely reflecting the wide range of techniques that fall within this category. While its risk of incurring side effects is minimal-to-moderate (e.g. itching, tickling and headache; Brauer et al., 2021; Zulauf-McCurdy et al., 2023), it has been shown to be costly (Lin et al., 2022; Chiu et al., 2022). Transfer effects need to be studied further at the requisite level.

Through various noninvasive techniques, this group of interventions has been shown to improve various primary and secondary symptoms of ADHD (e.g. hyperactivity, working memory deficits and selective attention abilities; Rajabi et al., 2019; Dobrakowski & Łebecka, 2019; Mishra et al., 2021). As stated above though, it is unclear whether these gains are sufficient to produce transfer effects in the form of academic outcome gains (Patil et al., 2022). The first author (RAR) found no QALY evidence for neurofeedback training versus treatment as usual (National Guideline Centre, 2018), though this technique is not likely to be covered by insurance (Corporate Medical Policy, n.d.).

This method has shown that the ADHD brain produces altered neural oscillatory signatures relative to controls. Coupling both recent findings showing a broad heterogeneity in the neural signatures of children with ADHD and limited spatial specificity of neuroimaging methods as they now stand (Hu et al., 2021), a notable amount of noise is introduced that muddles interpretation of its results. Given this variability (Luo et al., 2019), it may not be meaningful to hold even the mean trace as a neural pattern of central tendency (Drechsler et al., 2020); perhaps interpreting this population's "median trace" would be more meaningful. Further, "improving" the ADHD neural signature to mimic those of typically developing peers does not necessarily translate to improved functional outcomes (Bink et al., 2014), as recent conceptualizations of neurodiversity propose that blanket efforts to "normalize" atypical neural activity for normalization's sake should not be the goal of therapy (Spiel et al., 2022; Krakauer et al., 2017).

Non-immersive VR This technique is characterized by an un-occluded experience of manipulating a computerized avatar to perform a task. It is not expected to pose substantial risks to patient

safety (Corrigan et al., 2023). Secondary analyses are needed to clarify how impactful this intervention is between treatment groups, both on functionally similar and distinct tasks to the experimental one and how cost-effective the intervention is for patients and their families.

Though non-immersive VR is the most commonly employed VR design (Bassano et al., 2022), there are very few papers on this technique overall. Of the few that met the eligibility criteria, they have been used to improve many primary and secondary symptoms of pediatric ADHD (i.e. balance, cognitive control; Ou et al., 2020; Orkin Simon et al., 2020). The Food & Drug Administration (FDA) recently cleared EndeavorRX[™] as the first clinically relevant, prescription-based non-immersive VR for the cognitive training of children with ADHD (Pandian et al., 2021), improving children's ability to navigate a virtual environment while ignoring distractors and to multitask.

The FDA's administrative clearance is not necessarily founded on the tool's therapeutic potential though; Evans and colleagues (2021) highlighted the differences between the levels of scientific rigor necessary to gain FDA clearance and to create an evidence-based clinical treatment protocol, namely that the former sources much less heavily on RCTs. Further research is needed to ensure that this protocol produces meaningful results.

Semi-immersive VR This technique occludes patients' range of vision using a head-mounted display, such that they are immersed in a virtual environment that they can only interact with using real-world hardware like a keyboard or computer mouse. Studies using this technique exhibit a broad range of effect sizes (0.09 to 1.18; Roberts et al., 2021; Parsons et al., 2019), likely due to how well the virtual environment and task correspond to the ADHD symptom being

addressed. Further analysis is required to understand how this greater depth relates to task transfer and cost-effectiveness. As with non-immersive VR, this mode of VR is generally considered to be safe (Romero-Ayuso et al., 2021; Corrigan et al., 2023).

This intermediate level of immersion within a VR environment is either comparable or more effective than other treatment methods at improving behavioral outcomes (Bioulac et al., 2018). Training on a selective attention task resulted in improved task outcomes like an increased target hit rate and a decreased omission rate (Camacho-Conde & Climent, 2020; Coleman et al., 2019). Given the notably poor educational outcomes seen in a majority of children with ADHD (Calub et al., 2019), it is noteworthy that children with ADHD have shown improved outcomes in ignoring single- and multi-sensory distractors (e.g. students whispering to each other nearby while attending to a CPT being presented at the front of the classroom; Areces et al., 2018; Stokes et al., 2022; Yıldırım Demirdöğen et al., 2022).

While this technique is particularly useful for developing treatments for children with ADHD given their functional challenges, semi-immersive VR's main disadvantage is that it does not create the depth of the immersive experience that full immersion VR does (Huang et al., 2020; Baumann et al., 2020). Because users are only able to observe the virtual environment, they cannot enjoy the benefits of actively manipulating the environment as training for other tasks in the real world. Secondary analyses show that its development is moderately costly, though this technology is becoming more accessible especially as the requisite hardware and software it relies on improves (Parsons et al., 2015; Garner, 2017).

Fully immersive VR The fully immersive VR experience also occludes the physical environment, but it additionally allows interaction with the virtual environment though the use of haptic devices. Given that this method is not expected to evoke significant side effects and is not particularly costly (Corrigan et al., 2023), this may be a viable technique to use. However, without secondary analyses examining the effect size between experimental conditions, it remains unclear how useful this tool would be in alleviating atypical ADHD symptomatology. As this level of VR immersion most closely resembles the real-world environment, it is expected to produce the most generalizable outcomes relative to other VR techniques; Corrigan and colleagues (2023) recently proposed that VR may be a useful technique for producing carryover effects due to its interplay with cognitive functioning and social interaction abilities on academic performance, though the lack of studies at the other levels of immersion possibly makes this prediction premature.

Children with pediatric ADHD respond favorably to this technique (Huang et al., 2020); this should be capitalized upon as task engagement is a common limiting factor for this group. Though research in children is sparse, Alvarez-Suarez and Caldas (2023) found evidence of a near transfer effect in adults for whom the fully immersive VR training improved response impulsivity, compared to those who did the same task in the real-world. While these results are promising, further work needs to be done in children to determine if there is an effect of age.

A major disadvantage of this technique is that the requisite hardware itself can be an obstacle to a naturalistic immersion; Martin and colleagues (2021) found that the haptic devices and headmounted displays may restrict and occlude patients' gaze and movements, respectively, within the virtual environment. On the other hand, should the immersion be perceived as complete,

patients may erroneously apply the lack of bodily consequences within the virtual environment to the real world (Tiwari et al., 2022).

Augmented reality (AR) Augmented reality interventions utilize software that integrated the virtual and real-world environments. While information is sparse for the effectiveness of this intervention in children with ADHD, further research is needed on its cost-efficiency, task generalizability and to clarify this intervention's impact on patients. Secondary analyses are needed to clarify whether the heightened real world aspect maintains patient safety.

Theoretically, this method should be most effective of all the above techniques for gaining far transfer effect benefits, as it most closely translates between the virtual and real-world environments (Romero-Ayuso et al., 2021). It shows promise as being a powerful, wide-reaching educational tool by developing skills like improved task efficiency and emotional resilience (Ocay et al., 2018; Avila-Pesantez et al., 2018), though its modest results indicate that its paired methodology and application are not yet optimized. Barba and colleagues (2019) introduced a protocol where participants perform tasks on spatial reasoning, impulse control and action planning, allowing researchers to further probe how well behaviors trained within this highly ecologically valid method translate into generalized behavioral patterns. There is not a significant difference in how cybersickness is evoked between AR and VR in other clinical populations (Shahnewaz Ferdous et al., 2023).

With the radical popularity of consumer AR games, caregivers often report safety risks from children's engagement with the virtual objects that captures their attention away from hazards encountered in the real world. Guo and colleagues (2021) posited that use of augmented reality

comes with potential safety risks in motivating neurotypical adult users to focus on virtual elements over the real-world environment, though this also motivated them to adopt prophylactic behavioral changes to reduce their risk. As this study examined adults' behavior, it is necessary to do similar work in the population here studied, as they have an altered risk tolerance (Defoe et al., 2019).

General Discussion

While previous work sought to compare effectiveness across interventions, they did so by looking deeply at only one factor affecting the practical integration of a limited range of intervention techniques (i.e. Sampaio et al., 2021; Dijk et al., 2021). In the present scoping review, we sought to provide an overview of the diverse established and experimental intervention techniques currently used in clinical and laboratory settings, respectively, being implemented to ultimately alleviate the complex and heterogeneous symptoms of pediatric ADHD from several perspectives that contribute to a holistic view of the practical considerations needed to implement such a treatment.

Established interventions

First- and second-line interventions (neuropharmacology and psychosocial training, respectively) are commonly clinically used upon children's receipt of diagnosis. This is despite a highly variable degree of improvement between the treated and untreated groups (Idrees et al., 2022; Xue et al., 2019). While their generalizability from clinical intervention to real-world functional outcomes is unclear as a whole (Chan et al., 2023; Schneider et al., 2019), their risk of producing adverse

side effects is likewise variable (Pan et al., 2022; Barkley, 2018). And given that its costs may or may not be buffered for patients and their families (Sampaio et al., 2021; Payen et al., 2022), there is great motivation to develop alternative methods to incorporate into treatment plans to ameliorate these patients' symptoms.

Experimental interventions

A wide range of interventions (e.g. psychophysical and physical training, digital health applications, neuromodulatory training, virtual and augmented reality) are being tested for efficacy in potentially treating symptoms of child ADHD. This diversity in technique is reflected in a diversity of effect sizes between treatment and control groups (Westwood et al., 2021; Qiu et al., 2023), ability to translate to functional outcomes (Westwood et al., 2023; Ocay et al., 2018), financial burden to patients (where experimental interventions are seemingly less likely to be covered by insurers overall; Păsărelu et al., 2020; Lin et al., 2022), and risk of incurring side effects (Chen et al., 2022; Brauer et al., 2021).

Limitations

Though the reviewed factors (effect size, transfer effects, cost-effectiveness and risk of side effects) are critical for these interventions to effectively expand treatment options from the laboratory to the real-world, much research needs to be devoted to meet this goal. As a result of this marked lack of knowledge, the present work holds several limitations.

Only one author (RAR) reviewed the systematically searched papers such that inter-rater reliability could not be assessed. Additionally, publication bias may have been introduced through limiting our search to peer-reviewed papers written in the English language, reporting search results explicitly stated in the source material. Though this last property may have skewed results, this bias across papers is indicative of the literature's perspective on the given topics.

Though we targeted single-method experiments, we did not exclude those in which the patients used medications; this is not expected to have significantly skewed our findings, as they were part of the patients' baseline measurements. Moreover, we pooled results investigating these interventions' usage in both children and adolescents; though these populations are functionally similar (i.e. both populations attend grade school), they also hold functional and neurodevelopmental differences that call for separate analyses (Dow-Edwards et al., 2019). Given the sparseness of the source literature, this initial investigation paints broad strokes. Similarly, though we drew distinctions between the modes of VR, the literature often does not (i.e. Corrigan et al., 2023; Romero-Ayuso et al., 2021); by further reviewing the designs of papers they sourced from, we associated the qualitative evidence with the intervention interpreted to have been described.

While we constrained our included papers to those that compared the treatment group to a control group, as opposed to those making within-category comparisons, we did not restrict based on control design (i.e. active or passive). It may be argued that these diverse results are a by-product of inclusion of such a wide range of interventions; we did not specify a task because ADHD symptomatology is complex (Luo et al., 2019) such that alleviation efforts need to likewise
hold a high level of flexibility, especially when viewing the literature through an application-based lens.

We restricted our review of interventions' effect sizes to those using Hedges' *g*, which may be an overly restrictive criterion; we argue that the literature is relatively small, such that less bias is introduced when computing with this statistic that is adjusted for a small sample size compared to Cohen's *d*. As cost is reviewed here, the qualitative compilations do not allow for relative comparisons between interventions to be made. Cost utility for consumers through the quality-adjusted life year calculation may be a better metric to use, though it may be inappropriate, especially in relation to clinical populations (Harris, 1987).

Though these secondary analyses themselves drew from several sources, there is currently not sufficient data to draw reliable conclusions from the literature search. Moreover, other than the effect size factor, the other factors' results were not derived systematically despite being reported within secondary articles. Given that there are so few analyses at this requisite level, we do not posit that this work strongly recommends any one course of action. Since each method holds its own unique set of advantages and disadvantages, the optimal intervention is likely determined by the specific desired outcomes for a specific patient.

Future directions

While the present work is based on sparse results that do not yet provide a clear front-runner in intervention type for pediatric ADHD, it is noteworthy that computer-based training in its various forms is a major boon for developing potential therapies for pediatric ADHD (Liu et al., 2021). As

children with ADHD are driven to engage in computer-based tasks (Garner et al., 2008), it is possible that psychophysical training (and other interventions that integrate this method) may similarly prove to be a useful intervention for this population; direct research needs to be conducted to substantiate this claim.

Though VR is considered a monotherapy (Krzystanek et al., 2021), given that VR can be thought of as an agglomeration of several of the techniques described above that are each useful approaches to some extent, it is not surprising that meta-analyses of VR itself show promising results that prompt further investigation (Roberts et al., 2021; Parsons et al., 2019; Romero-Ayuso et al., 2021). Because VR training implicitly integrates multiple behavioral patterns simultaneously, it can be expected that it has greater efficacy in multiple domains as compared to other more singular methods (Takacs & Kassai, 2019). This allows both a flexibility and specificity unique to this method imbued through the particular parameters employed.

Though more work needs to be done in VR on the whole and at deeper levels of immersion specifically (Bassano et al., 2022), increasing depth of immersion is associated with a reported increase in subjective experience of immersion within the virtual environment, an increase in motivation to complete a task and reported symptom alleviation by caregivers that is corroborated by improvements in various outcome measures (i.e., failures of omission and commission; Huang et al., 2020; Eom et. al., 2019; Clifford et al., 2018; Baumann et al., 2020). This may be because the additional stimulation of the VR experience compared to another method with less immersion heightens alertness from ADHD patients' baseline hypoarousal level, thereby enhancing task engagement (Geissler et al., 2014; Berger et al., 2021; Muna et al., 2021). The degree to which patients are affected by increasing their stimulation levels is still unclear (Berger & Cassuto, 2014;

Allen & Pammer, 2015; Hulac et al., 2020), calling into question this proposition (Baijot et al., 2016).

As a whole, this novel, digitally-based, and non-invasive technology that builds on the techniques of other tools carries several potential risks and limitations uniquely associated with integrating VR into a treatment plan for children with ADHD. Patients have reported cybersickness (Kim et al., 2014) that increases with depth of immersion after extensive use of virtual reality (Martirosov et al., 2021); this has largely not been supported by systematically controlled studies though (Nolin et al., 2016; Servotte et al., 2020). There is an additional risk of children utilizing this device for a longer duration than it is healthy to interact with a screen; since children with ADHD may be at greater risk than their typically developing peers at developing such an addiction (Tamana et al., 2019; Kietglaiwansiri & Chonchaiya, 2018), this underlines the importance of presenting this tool within structured protocols. Further, VR results must be cautiously interpreted through the lens that its literature is often rife with methodological problems, such as small sample sizes and inappropriate statistical analyses (Evans et al., 2020).

While there is a need for caution when integrating any novel technique into a clinical treatment plan, VR is a potentially powerful and evermore practically utilized, but understudied, tool for the evaluation and possible therapeutic remediation of the atypical and adverse symptoms seen in children with ADHD (Lakes et al., 2022; Parsons et al., 2019), relative to other more traditional interventions. This method has become a viable and promising option to integrate into therapeutic regimens by targeting the core symptoms of ADHD with better ecological validity than other common experimentally controlled techniques (Parsons, 2015; Seesjärvi et al., 2022; Roberts et al., 2021). Importantly, this tool is particularly powerful in facilitating task completion, as its

characteristic gamified presentation elevates children's motivation where treatment adherence is often low (Dekkers et al., 2017; Biederman et al., 2019). VR is known to alter the perception of time (Ghomi, 2018), which is especially interesting to probe and potentially improve upon given that temporal dysregulation is a marked secondary symptom of ADHD (Ptacek et al., 2019).

Combination therapy is known to produce better results than monotherapies; Garcia Pimenta and colleagues (2021) show that the efficacy overall for a combined treatment of the established interventions (neuropharmacology and cognitive training) is greater than either treatment in isolation. At this time, most multi-pronged treatment plans combine these two techniques, although considerable effort is underway to expand the range of options afforded by also incorporating some of the experimental monotherapies reviewed above (Lin et al., 2022). Further work should examine whether combining interventions will have additive effects (e.g. VR and neurofeedback; Blume et al., 2017).

It remains to be seen how ADHD subtype, behavioral task and level of VR immersion interact; though sufficient attention has not been paid examining which ADHD subtype is best-suited to be targeted by each intervention (and which symptom is best-targeted), analysis at this level of granularity can inform which specific VR technique will be most efficacious in producing optimal outcomes that can be developed into more targeted and effective treatment protocols (Mueller et al., 2017). More research is needed to investigate the generalizability of VR-gained outcomes to ascertain its broader usefulness in providing symptom relief. While the relatively low technological barrier and level of invasiveness that VR presents (though it's steep price of development and potential risk of reinforcing problematic behaviors (e.g. overuse of technologies tempers its feasible applicability; Werling et al., 2023), it can be applied in non-clinical settings

(e.g. at school; Perone, 2016) to further integrate behavioral interventions into patients' daily lives to provide a more holistic symptom relief.

Conclusion:

By reviewing the literature on the advantages and disadvantages of each intervention, we provide context for the methodical search of several factors crucial to their integration into effective treatment plans for this large patient population. The standard modes of intervention (i.e. medication, cognitive therapy) have produced modest effects in alleviating the adverse symptoms of ADHD when used in isolation, suggesting that additional techniques need to be integrated into the array of treatment options. While there is much work yet to be done to elucidate these efficacies, carefully incorporating these novel tools into treatment plans may be the catalyst to progress patient outcomes beyond what current therapies provide. Taking a precision therapy approach may be most effective for addressing the individualized needs of this heterogeneous population.

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