Section 2: English Abstract

Full title of research project

Improving identification and distinguishability of medication labels

Investigators: full name and affiliations

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Key Words

Medication Safety, Drug labelling, Spatial Frequency, Visual Patterns, Patient Safety.

Abstract

An abstract of up to **300 words** should include these headings: (1) Scientific Background (2) Objectives (3) Methodology (4) Findings (5) Conclusions (6) Policy Implications / recommendations

Background: Errors during medical treatment occur at a high rate and are considered to be one of the leading causes of death in developed countries. One of the most common types of medical errors is medication error.
Objectives: This study investigates the use of visual patterns as a means of improving medication identification when providing medicine. We developed labels divided according to the spatial frequency index of the background, and we used them for an experiment to test if the patterns were able to provide performance improvements beyond text labels in a search and recognition task.
Methodology: The experiment compared three types of labels: white labels and two types of patterned labels. We designed 75 labels of two types, 30 white and 45 patterned labels, which included 30 low spatial frequency labels and 15 high spatial frequency labels. The experiment included 60 participants where 20 participants experienced each of the label types.
Findings: Our results reveal significant differences between use of the labels both in response time and accuracy. The average response time for the patterned labels was 2,810 ms with the low spatial frequency labels, and 3,477.62 ms with the high-low spatial frequency labels, compare to 4,410.56 ms with the white labels ($p<0.05$). The accuracy of the patterned labels was 80.5% and 74.7% with the white labels. We also found differences in the search pattern for the patterned labels compare to the white labels .
Conclusions: Results indicate that adding patterns to the background of text labels significantly reduced search times, and improved accuracy. These results suggest that patterned labels can reduce search time and may reduce the likelihood of errors.
Recommendations: The use of visual patterns as background that were evaluated in this study present promising potential for a new approach in improving medication identification. Our recommendations suggest that policy makers should consider the use of such solution as part of future standard for medication labeling.

Section 3: Hebrew Abstract

כותרת מלאה של המחקר

שיפור הזיהוי והמובחנות של תוויות לסימון תרופות

חוקרים: שם מלא ושיוך מוסדי

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מילות מפתח

תוויות לסימון תרופות, בטיחות הטיפול, דגמים גרפיים, תדירות מרחבית, בטיחות במתן תרופות

תקציר

תקציר שאורכו עד **200 מילים**, אשר יכלול כותרים אלה: (1) רקע (2) מטרות (3) שיטה (4) ממצאים עיקריים (5) מסקנות (6) המלצות / השלכות לקובעי המדיניות

רקע: טעויות במהלך הטיפול הרפואי מתרחשות בשיעור גבוה ונחשבות לאחת מסיבות המוות המובילות במדינות מפותחות. אחד הסוגים השכיחים ביותר של שגיאות רפואיות הוא שגיאות במתן של תרופות.
מטרות: המחקר בדק שימוש בדגמים גרפיים (PATTERNS) כאמצעי לשיפור הזיהוי של תוויות של תרופות. פיתחנו תוויות הנבדלות בתדר המרחבי של הרקע (spatial frequency), וערכנו ניסוי שבדק אם הדגמים הגרפיים מספקים שיפורים בביצועים לעומת תוויות טקסט במשימת חיפוש וזיהוי.
שיטה: הניסוי השווה בין שלושה סוגים של תוויות: תוויות לבנות ושני סוגים של תוויות עם דגמים גרפיים - עם תדר מרחבי נמוך ועם תדר מרחבי גבוה. בניסוי השתתפו 60 משתתפים, 20 בכל אחת מסוגי התוויות.
ממצאים: קיימים הבדלים משמעותיים הן בזמן תגובה והן ברמת הדיוק. זמן התגובה הממוצע עבור התוויות התדר המרחבי הנמוך היה 2,810 מילי-שניות, ו- 3,477.62 מילי-שניות עם תוויות התדר המרחביות הגבוהות, לעומת 4,410.56 מילי-שניות עם התוויות הלבנות ($p < 0.05$) . הדיוק בזיהוי התוויות עם הדגמים גרפיים היה 80.5% לעומת 74.7% עם התוויות הלבנות. נמצא הבדל בדפוס החיפוש עבור התוויות עם דגמים גרפיים בהשוואה לתוויות הלבנות - החיפוש אחר תוויות לבנות נעשה בעיקר לאורך ולרוחב, ואילו החיפוש אחר תוויות עם דגמים גרפיים נעשה גם באלכסון.
מסקנות: מהתוצאות עולה כי הוספת דגמים גרפיים לרקע של תוויות טקסט הקטינה משמעותית את זמני החיפוש ושיפרה את הדיוק.
המלצות: שימוש בדגמים גרפיים יכול להקטין את הסבירות לטעויות במתן תרופות.

Section 4: Executive Summary- Hebrew

רקע מדעי:

טעויות במהלך הטיפול הרפואי מתרחשות בשיעור גבוה ונחשבות לאחת מסיבות המוות המובילות במדינות מפותחות. אחד הסוגים השכיחים ביותר של שגיאות רפואיות הוא שגיאות במתן של תרופות. מחקרים של Reason, 1990 מראים שטעויות במהלך ביצוע עולות שגרתיות יכולות לקרות לכל אחד, אולם Aronson 2009 הציע להקטין את ההסתברות לטעויות במתן תרופות באמצעות שיפור הסימון של התרופות. בעשור האחרון נעשו מספר ניסיונות לשיפור סימון תרופות (לדוגמה Porat, Bitan, Shefi, Donchin & Rozenbaum, 2009).), אולם אף אחת מהשיטות שהוצעה לא אומצה בהצלחה.

מטרות המחקר:

מחקר זה בודק את השימוש בדגמים גרפיים (PATTERNS) כאמצעי לשיפור הזיהוי של תוויות של תרופות. לצורך המחקר פיתחנו תוויות המסומנות בדגמים גרפיים ייחודיים הנבדלים בתדר המרחבי שלהם (spatial frequency). באמצעות ניסוי שהתבצע עם סטודנטים באוניברסיטת בן-גוריון בדקנו את דיוק הזיהוי, מהירות הזיהוי ואופן הסריקה אחר התווית בין תוויות עם תדר מרחבי שונה, ותוויות לבנות (ללא הדגמים הגרפיים).

שיטות:

הניסוי השווה בין שלושה סוגים של תוויות: תוויות לבנות ושני סוגים של תוויות עם דגמים גרפיים. עיצבנו 75 תוויות משני סוגים, 30 תוויות לבנות ו - 45 תוויות עם דגמים גרפיים, שכללו 30 תוויות עם תדר מרחבי נמוך ו - 15 תוויות עם תדר מרחבי גבוהה. הניסוי כלל 60 משתתפים, 20 משתתפים בכל אחד מסוגי התוויות (מערך ניסוי בין נבדקי). כל נבדק הגיע לשלושה מפגשים – בשני המפגשים הראשונים הוא התנסה במשחק במהלכו הנבדקים הכירו את התוויות השונות לפי תנאי הניסוי אליו הם שוייכו; המפגש השלישי נועד לבדוק את הדיוק ומהירות התגובה של הנבדק בזיהוי תוויות שונות. במפגש השלישי נעשה גם שימוש במערכת מעקב אחרי תנועות עיניים שאפשרה לנו לבדוק את אופן הסריקה אחר תווית בתוך מערך של תוויות.

ממצאים:

התוצאות חושפות הבדלים משמעותיים בשימוש בתוויות הן בזמן תגובה והן ברמת הדיוק. זמן התגובה הממוצע עבור התוויות בתדר המרחבי הנמוך היה 2,810 מילי-שניות, ו- 3,477.62 מילי-שניות עם תוויות התדר המרחביות הגבוהות, לעומת 4,410.56 מילי-שניות עם התוויות הלבנות ($p < 0.05$) . הדיוק של התוויות עם הדגמים גרפיים היה 80.5% ו 74.7% עם התוויות הלבנות. מצאנו גם הבדלים בדפוס החיפוש עבור התוויות עם דגמים גרפיים בהשוואה לתוויות הלבנות, כאשר החיפוש אחר תוויות לבנות נעשה בעיקר לאורך ולרוחב טבלת התרופות, ואילו החיפוש אחר תוויות עם דגמים גרפיים נעשה גם באלכסון .

מסקנות:

מהתוצאות עולה כי הוספת דגמים גרפיים לרקע של תוויות טקסט הקטינה משמעותית את זמני החיפוש ושיפרה את הדיוק. תוצאות אלה מראות שתוויות בדוגמאות יכולות להפחית את זמן החיפוש ועשויות להפחית את הסבירות לטעויות.

המלצות:

החשיבות של הקטנת מספר הטעויות במתן תרופות, והצורך בתקנים לסימון תרופות קיים שיגרמו להקטנה ההסתברות לטעויות – ידועים. המחקר הנוכחי הראה כיצד ניתן להגיע לזיהוי טוב יותר באמצעות סימון פשוט ואפקטיבי. ההמלצה שלנו היא ששיטת הסימון שנבדקה תהווה חלק מהתקן המתהווה לסימון תרופות, ובכך תתרום לשיפור בטיחות הטיפול.

מקורות:

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Porat, N., Bitan, Y., Shefi, D., Donchin, Y., & Rozenbaum, H. (2009). Use of colourcoded labels for intravenous high-risk medications and lines to improve patient safety. BMJ Quality & Safety, 18(6), 505–509.

Reason, J. (1990). Human error. Cambridge University Press.

Section 5: Comprehensive scientific report – English

1. Scientific background

Medication Errors

Error is a circumstance in which planned actions fail to achieve the desired outcome (Reason, 1990). This is usually the result of latent conditions that together with human limitations translate into active failures. He suggested classifying errors into two main categories:

Rule-based mistakes involve a higher level of mental processing. These include planning, decision making, and inadequacy of judgment.

Action-based errors are slips and lapses at the execution level that usually happen in routine and sequential tasks.

One of the most common types of medical errors is medication error (Bates et al., 1995). It is also the single most preventable type of error (Aspden et al., 2007). A medication error is defined as any error in the administration of a medication, regardless of whether the error causes adverse effects or not.

Aronson (2009) adapted Reason's error classification for medication errors. He argued that **action-based errors** (Slips at the execution level) are best exemplified by picking up an ampule of diazepam from the ward pharmacy shelf, while looking for diltiazem. These can be minimized by avoiding distractions, by cross-checking, and by careful and good labeling.

Dispensing errors can occur at any stage of the dispensing process, from the receipt of the prescription at the pharmacy to the supply of a medicine to the patient. Studies investigating medication dispensing errors show large gaps in the number of errors. Dispensing errors occur at a rate of 1–24 % and also include selecting the wrong strength or product (Allan et al., 1995; Flynn, Barker, & Carnahan, 2003). Flynn et al. (2003) found that dispensing errors occurred at an average rate of 4 in 250 prescriptions (1.6%) in pharmacies in the United States. Cheung et al. (2009) found that dispensing error incidents up to 45% were reported in different pharmacy settings.

In order to understand why such errors occur, it is first important to understand the workflow and cognitive processes pharmacists go through when selecting a specific medication. Pharmacists received a level of training to determine the specific medication and dosage required correctly. Additionally, they will have a mental image of where that medication is located and what it looks like. They will then turn their attention to the vicinity in which they anticipate finding the medication and select it from its probable location. After that, before administering the medication, they will visually check to confirm that it is the correct and intended medication. If the pharmacist is going to perform a visual triple-check of the medication prior to administering it, the first check is when the medication is pulled or retrieved from the automated dispensing machine, the medication drawer, or whatever system is in place at a given institution. The second check is when preparation of the medication for administration takes place. The final check, before giving the medication, is to check the prescription label against the medication log entry again to make sure that they match. One might argue that the final check should negate the need for additional precautions, but this argument assumes ideal conditions and an ideal world in which checks are always performed correctly, and any errors are always detected.

Confirmation bias can result in pharmacists incorrectly confirming medications during visual checks, based on the expectation that they have correctly selected the intended medication. Poor lighting conditions may also cause pharmacists to inadequately perform checks, while stressful situations may cause them to skip checks altogether in response to a perceived lack of time due to treatment urgency (Beso, Franklin, & Barber, 2005). Finally, the presence of look-alike (and perhaps to some extent sound-alike names of medications that have spelling similarities and/or similar phonetics) medications can increase the difficulty of accurately performing checks. One-third of incidents were associated with confusion of similar medication names, and nearly half were associated with medication strength confusion (Cheung et al., 2014). Medication name and strength confusion are serious issues as they are preventable with a potential detrimental impact on clinical practice and patient safety (Emmerton & Rizk, 2012; Ostini et al., 2012). This confusion pharmaceutical intensity can occur when two strengths of the same medication look the same: for example, 3.75 mg and 0.375 mg of pramipexole (Anto et al., 2011).

Reducing Medication Errors

There is more than one way to reduce medication errors. One of these ways is improving the readability and understanding of medication instructions. Instructions are often vague and require patients to make inferences regarding how to correctly self-administer them, a task that is consistently difficult for patients with low health literacy (Wolf et al., 2007). In addition, medication instruction is rarely available in languages other than English, placing patients with limited English proficiency at greater risk of misunderstanding medication instructions and warnings (Bailey et al., 2009; Bradshaw, Tomany-Korman, & Flores, 2007; Leyva, Sharif, & Ozuah, 2005; Sharif, Lo, & Ozuah, 2006; Weiss et al., 2007). Medication errors include not only therapeutic medications, but also include production or assembly, prescription, transcription, distribution and administration of a medication, and monitoring its effects afterwards (Aronson, 2009). Improving the readability and understanding of instructions for prescription medications is necessary, as this may ultimately stimulate appropriate and safe medication use among patients (Hernandez et al., 2008).

Poorly designed labels pose a threat to patient safety by contributing to medication errors. Nearly one-third of the errors reported to the United States Pharmacopeia (USP) cited labeling or packaging issues (United States Pharmacopeia, 1998). Clutter, poor readability, poor use of color, and lack of differentiation between similarly-named medications are among the labeling concerns reported. In a self-reported survey, anesthesiologists cited the misidentification of a syringe and the misidentification of a medication ampoule or vial as a contributing factor in 70.4% and 46.8% of medication errors they experienced, respectively (Orser, Chen, & Yee, 2001).

Medication Labeling

The labeling of medications encompasses the provision of information and instructions to ensure safe and effective use of the products by patients. While the labels of dispensed medications represent one of the most important sources of information available to patients (Hernandez et al., 2008; Neoh et al., 2009; Shrank et al., 2007), prescription medication labels are not currently designed in a patient friendly way. Legitimately, labeling information includes, but is not limited to, the following categories: patient identification, medication name, dosage, frequency, route of administration, production and expiration dates, and some medication storage requirements (Brown-Brumfield & DeLeon, 2010). However, medication labeling in actual practice is almost always inconsistent, incomplete,

or difficult for patients to understand (Orser, 2000; Shrank et al., 2007). This vague information is a clear cause of medication errors (Aspden et al., 2007; Bootman et al., 2006). Health literacy and language concordance as medication safety concerns is essential in understanding the need for and design of enhanced medication labeling. Standardizing medication labeling is an important step towards ensuring equity in patient access to clear, concise, and consistent prescription medication information (Aspden et al., 2007; Hernandez et al., 2008). Confusing names, labels, sound-alike and look-alike medication names, and packaging increase the risk of unintended interchanges of medication that can result in serious complications, and even death. Labels that are hard to read can also contribute to errors (Canada, 2004; Rataboli et al., 2005).

Hospitals and healthcare professions have developed elaborate pharmacy and nursing practices in an attempt to circumvent such errors. Pharmacists and nurses are extensively trained and tested for proficiency in safe medication practices. For example, they are taught to always read the label carefully and to have dosage calculations double-checked by another person. Physicians, as learned intermediaries with legal responsibilities to instruct patients on prescription medication use, frequently miss opportunities to counsel patients on how to take prescription medications (Tarn et al., 2006). Pharmacists, at the point of dispensing medicines, also do not often communicate detailed information to patients to support their compliance with prescribed regimens (Morris, Tabak, & Gondek, 1997).

Unsurprisingly, errors still occur. According to a (2007) Institute of Medicine report, poorly designed prescription medication labels were identified as an important source of medication errors. The USP reports that approximately one-third of errors it evaluates are, at least in part, because of confusion caused by product labeling (Berman, 2004). This was also reported in a 1995 study of adverse medication events (ADEs) (Bates et al., 1995) at the Brigham and Women’s Hospital and the Massachusetts General Hospital, which had an estimated 1,600 serious medication errors and 500 adverse medication events that year. The problem is that even the best trained and most careful people occasionally make mistakes. No human can function perfectly all the time. Therefore, the system needs to support the human that use it.

Studies show that careful design of objects and procedures can make a huge difference in whether errors will occur. Simplicity, standardization, differentiation, lack of duplication, and unambiguous communication are some of the human factors that are relevant to the medication use process. These principles have often been ignored in the naming, labeling, and packaging of medications. The consequences are predictable. Confusing names, along with poor labels and packaging represent accidents waiting to happen (ISMP Canada, 2004; Ciociano & Bagnasco, 2014; Rataboli, Garg, & others, 2005). Kohn et al. (2000) noted that one reason for the magnitude of medication-related errors was that "medication may be prone to error in use due to sound-alike or look-alike names, unclear labeling, or poorly designed packaging," but that the percentage of errors and injuries caused by faulty names and labels is unknown and hard to estimate. A report by USP (2004) indicated that confusion over medication names accounted for 15% of errors from January 1996 through December 2000. The same report lists 749 medication names reported to Medication Error Reporting Program (MERP) because they sound alike when communicated orally or look-alike in print or when written. Approximately 25% of medication errors are related to name confusion and another 25% to labeling and

packaging issues. The Institute for Safe Medical Practices (ISMP) estimates that only 1–2% of events are even reported. Thus, the total number of patients who are injured or die annually because of medication name confusion is probably at least 10,000 and could be twice as high. A similar number are injured as a result of errors caused by confusion attributable to labeling and packaging (Canada, 2004).

Today there is no uniform standard between manufacturers for how medications should be labeled. As a result, an adrenaline vial manufactured by one manufacturer may be packaged and labeled entirely differently from the same medication manufactured by another company. Similarly, one manufacturer may package and label an atropine vial in a way that is very similar to the packaging and labeling made by another manufacturer for adrenaline. Lack of such a standard adds to confusion and may be a major contributor to errors during administering medications at home and in various medical institutions.

Another source for error might be related to the fact that people read words as a single unit (Ehri, 2005); therefore, they pay little attention to small spelling differences. Often medication errors stem from misidentification and misdiagnosis of the conditional medication (Bates et al., 1995). Labeling and packaging design were recorded as a contributing factor to error in 21%–33% of all medication errors (Berman, 2004; Orser, 2000). Improving the identification and differentiation between medication packaging or varied doses and concentrations of the same medication may assist in reducing use errors made by medical staff (physicians, nurses, paramedics, and pharmacists) and errors made by patients who take several medications at home (an aging population that uses medications regularly) (Berman, 2004). Thus, it is essential to define label design characteristics that will improve identification and differentiation between pharmaceutical packaging.

Medication labeling improvements

After evaluating the errors resulting from the design label, several approaches tried to improve medication identification with partial success. These include three types of approaches: (a) *color coding* of medication labeling and *label format* (Institute for Safe Medical Practices, 2003), (b) *readability* and improved decoding of medication labels (Through "Tall Man", bold font) (Filik et al., 2004), and (c) *label design* that encoded the pharmacological properties of the medication (Porat et al., 2009).

Visual patterns

While the color spectrum might appear vast, in reality, there are perceptual limitations that severely limit the number of colors that can effectively be coded to items. On the other hand, visual patterns, such as checkerboards or polka dots, may not be as constrained. Of course, it is still necessary to ensure that enough distinction exists between any two patterns used, such that they can be distinguished from one another.

An understanding of pre-attentive processing (i.e. perception that does not require intentional cognitive resources) may partially explain why some patterns are more distinguishable than others, and why humans are able to quickly and easily distinguish one visual texture from another. Thus, it is necessary to understand the different relevant theories in order to know which patterns capitalize on these capabilities.

According to Treisman and Gelade (1980), selective attention and behavioral delay are two sides of the same coin: attention is the effect of competition bias in favor of task-relevant information, whereas delay is the result of irrelevant information. This allows one to capture certain features or characteristics (e.g. color, line length, and orientation) early,

automatically, and simultaneously. However, the ability to customize a given feature for processing individually also depends on the composition of the other fields. That is, a red circle is easily processed separately between a field of blue squares; however, the same red circle is much less clear between a sea of red squares. Color, size, orientation, contrast, and glamour are some of the features that can be processed individually. Treisman (1980) described each of these features as being processed into unique “maps” separately and simultaneously. Thus, comparing differences is a relatively simple task that involves comparing different maps, and humans are able to quickly and easily differentiate between each other's visual fabric when perception does not require deliberate cognitive resources.

Similar to the feature integration theory, the guided search theory, proposed by Wolfe et al. (1989), also proposes that the processing of different features occurs independently and in parallel. However, Wolfe et al. incorporated an additional top-down element in which particular features of the target element in question can be activated within the map locations, making search tasks more efficient. Thus, when searching for a red circle among a field of red Xs and green circles, it is possible to ignore all non-red items, as only the map(s) associated with the color red would be activated. In other words, the search is guided towards red elements as a result of the activation of the red color map which promotes perception of the red elements.

Similarly, using visual patterns that contain features that can be activated in a similar manner, it might be possible for users to guide their searches based on particular pattern features. For example, when looking for a pattern with diagonal lines, it might be possible that the search is guided or focused, such that patterns that contain diagonally-oriented primitives are perceived more prominently than patterns that do not contain diagonal features.

A study by Fukakusa (2018) indicates that the addition of patterns in the background of text-based labels significantly reduced search times and improved identification confidence, with no apparent loss of accuracy. The study was based on the use of spatial frequency to classify the level of complexity of the labels it used. This suggests that patterns designed in accordance with human perceptual capabilities can reduce search times and potentially reduce the possibility of errors based on label misidentifications.

Spatial frequency

To compare and measure the patterns we use, we needed a tool that could measure the abstract patterns we developed. One way to measure patterns is through spatial frequency. This is defined as "the number of pattern cycles per unit angle (usually degrees) subtended by the eye" (Ware & Knight, 1995). In reality, within a given image, a near infinite number of frequencies exist; thus, the definition of spatial frequency above more accurately refers to the most dominant frequency present. The dominant spatial frequency typically corresponds to the repetition of the most basic primitive element. For example, a high spatial frequency implies a short distance between adjacent bars and, hence, represents a stimulus of high detail. Based on similar definitions, spatial frequency can be considered somewhat related to Rao & Lohse's (1996) dimension of repetitive versus not repetitive design.

The spatial frequency was calculated using Matlab. A 2D Fast Fourier Transform (2D FFT) on each of the pattern images was used in order to produce a gray-scale magnitude spectrum image containing the spatial frequency characteristics of each original image. For

improved clarity in the images, the “fftshift” Matlab function was applied to relocate the DC component to the center of the image. The magnitude in the transform represents the contrast in the original image at the frequency level given by the F (u) and F (v) coordinates (i.e. in the x or y directions, respectively). Higher contrast indicates a stronger presence of that frequency component in the image. Lower frequency components appear as white values closer to the center, while higher frequency components appear as white values towards the edges. The most intense white value will appear in the exact center of the image, and will correspond to the most dominant spatial frequency.

To scale the axes and extract spatial frequency values from the magnitude spectrum in cycles per degree, the origin was re-centered at the 0 cycle/degree DC component, and the axes units were converted to cycles per visual degree by dividing by the size of the image in visual degrees. The size of the image in degrees was determined using the following equation, along with a measurement of the patterns as they were displayed on the screen (84.6 mm x 52.9 mm), and the estimated viewing distance of 630 mm

$$\text{Visual Angle (in degrees)} = 2 \times \operatorname{atan}\left(\frac{image\ size}{2 * viewing\ distance} * \frac{180}{\pi}\right)$$

The dominant spatial frequency was predicted to affect the distinguishability of visual patterns based on the idea that the dominant spatial frequency can affect the level of detail of the label background. For example, in low spatial frequency, the label will not be too complex and overloaded with drawings to affect its distinguishability. We use the spatial frequency ranking to characterize patterns that we use in our experience.

Studies of attention in visual search have demonstrated, through measurements such as reaction time and accuracy (percent correct), that spatial frequency can indeed guide visual attention (Sagi, 1988; Treisman & Gelade, 1980; Wolfe, 2015; Wolfe & Horowitz, 2004).

Further psychophysical studies have shown that spatial frequency is an important feature in visual processing, generally using contrast sensitivity (Campbell & Robson, 1968; Graham & Nachmias, 1971).

Visual search

Visual search can simply be defined as the task of looking for objects of interest in cluttered visual environments. The importance of incorporating eye movements to study observer strategies in a visual search has been emphasized in recent years (Findlay et al., 2003; Geisler, Perry, & Najemnik, 2006; Rajashekar, Bovik, & Cormack, 2006; Zelinsky & Sheinberg, 1997). According to physiological studies, nerve cells at different stages of the visual pathway are selective for spatial features and orientation of visual stimuli (Enroth-Cugell & Robson, 1966; Kuffler, 1953). This can lead to using a different search method with a spatial frequency label compared to other labels.

2. Research Objectives

The motivation for the current research was to investigate the viability of using visual patterns to improve medication label identification. We defined visual patterns as a primitive graphical element or feature repeated according to a particular rule to form a visual pattern. We hypothesized that visual patterns will increase the visually identifying characteristics and, thus, reduce the likelihood of slips and lapses type errors occurring. To our knowledge, no study has been conducted to evaluate the use of visual patterns to improve medication identification. Thus, the goal of the current study was to examine new medication label design characteristics that will improve the identification and differentiation

of medications, thereby reducing medication errors in medical institutions and people's homes. More specifically, our study examined whether the addition of patterns as a background to medication names would help people to more accurately identify them. We expected that adding distinctive features such as consistent visual patterns to medication labeling would cause those labels to appear more distinct from one another, and that such differences would decrease the probability that medications would be visually mistaken for one another. The results of the research will help the healthcare system improve the design of medication labels to reduce the number of medication errors.

Hypotheses

We hypothesized that there are specific visual pattern design features (measured by spatial frequency ranking) whose application in the labels' background would have a significant impact on the speed and quality of label identification.

• Hypothesis 1A: **Response times** to labels with a visual pattern in the background will be short compared to a label without a background.

• Hypothesis 1B: **Response times** to labels with a visual pattern with a low spatial frequency ranking will be shorter than those with high spatial frequency.

• Hypothesis 2A: **Accuracy** of identifying labels with a visual pattern in the background will be better compared to a label without a background.

• Hypothesis 2B: **Accuracy** of identifying the labels with a visual pattern that has low spatial frequency will be better compared to a label with high spatial frequency.

Hypothesis 3: The properties of visual patterns will affect the **visual scanning method**. The patterns will allow participants to search more efficiently, “jumping” between patterns, compared to searching when all the labels are white.

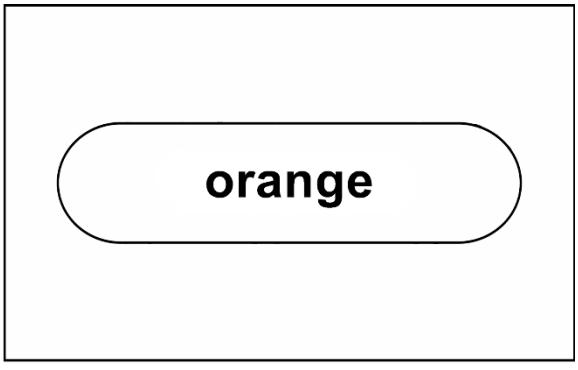
3. Methodology

Overview

The experiment was designed to test whether the addition of visual patterns to text labels could provide a complementary means of improving identification beyond the use of text alone. It was designed around a task similar to that used by Irwin et al. (2013), in which participants were presented with a target label for a short period of time, after which they were asked to identify the target from an array of similarly designed labels. The current experiment followed this model, that is, a trial consisted of a brief target label presentation, followed by a search task. Participants were first shown the name of the target label, followed by a search task in which they were asked to identify their target from a set of 30 alternate labels.

In order to test the experimental hypotheses, it was necessary to have white-background labels on which to form baseline measurements, and onto which patterns could be added to observe any effects that adding these patterns might have. Thus, the experiment compared three types of labels:

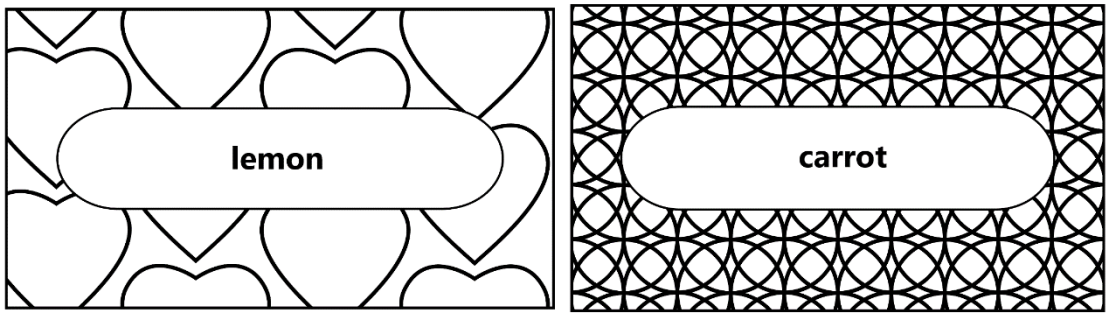
White Labels—These had a text box with a white background.



White label

Patterned Labels—These incorporated visual patterns with text boxes used in the white

labels condition, to create labels with background visual patterns (both low and high spatial frequency labels).



Low Spatial Frequency Patterned Labels—These were patterned labels with low spatial frequency patterns only.

We designed 75 labels of three types in a size of 320 x 200 pixels: 30 white labels and 45 patterned labels, which included 30 low spatial frequency labels and 15 high spatial frequency labels. All three label types had the medication name in the center. As the participants of this experiment did not have a clinical background, the titles of the labels were names of fruits, vegetables, and animals. The titles were chosen from the English Lexicon Project that has a range of 2–3 syllables, a word frequency between 6.5–10, and word lengths of 4–7 letters to neutralize the effect of syllables and frequency on identifying labels (Balota et al., 2007).

Participants

Participants were 60 second- and third-year Industrial Engineering & Management students at Ben-Gurion University of the Negev. They were randomly assigned to each of the three conditions (20 students in each condition). Participants were recruited through the students' internet message board, and they received a bonus mark in one of their courses. The study was conducted at the HSI laboratories at university, and was approved by the ethics committee there (#1772-1).

Apparatus

The experiment was developed using OpenSesame software designed for creating experiments in psychology and neuroscience (Mathôt, Schreij, & Theeuwes, 2012). Wherever the basic abilities of OpenSesame were inadequate for experimental purposes, Python scripts were created to supplement functionality.

In addition, we used the Tobii Pro Glasses 2 Eye Tracking System to capture participants' eye movements during the search task.

Procedure

The experiment was divided into three parts – two for training and one for data collection. A set of 20 labels with titles was created for each participant, where the titles were randomly assigned to the backgrounds. For each participant, the set of labels with the titles were used throughout all three parts of the experiment. Participants were seated in a quiet room in front of a DELL computer 63 cm away from a 24-inch screen with a resolution of 2560 x 1440 pixels.

The first part was a learning phase. Participants learned the 30 labels by playing a memory game. In this game, participants were asked to find 30 pairs of labels in two stages, 15 pairs in each stage. They were presented with an array of 30 blank labels and asked to click on two labels to find identical pairs of 15 labels (see Figure 1-Stages of Game 1).

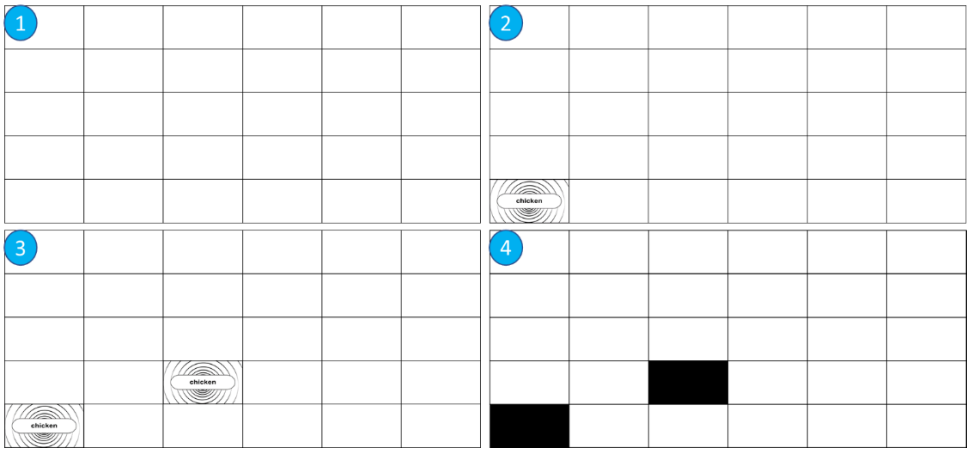


Figure 1-Stages of Game 1

In the second part, participants were asked to find 30 label titles from the set of labels. In each step they were presented with a label title (e.g. eagle); then they were presented with a set of 30 label backgrounds for two seconds; afterwards, participants were presented with the set of labels with backgrounds and titles for seven seconds and were asked to identify from the array the label title shown at the beginning (see Figure 2-Second Game).

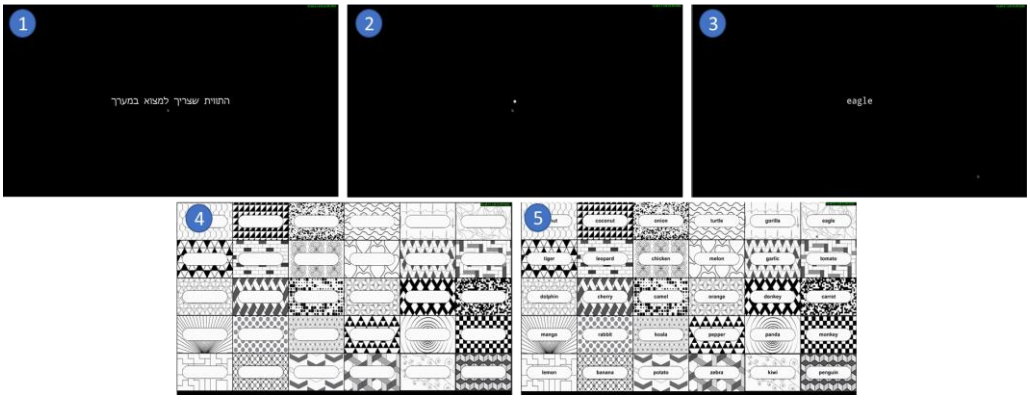


Figure 2-Second Game

In the last part, participants used the Tobii Pro Glasses 2 eye tracking device. At the beginning of this part, a short calibration task was conducted. Participants were presented with a label title in the center of the screen for five seconds. The participant had to memorize it, and then locate it within the perceptual array of 30 labels. The presentation of the target was followed by a fixation point for three seconds before the perceptual array was shown for seven seconds. When participants located the target within the perceptual array, they clicked on the label containing the target and then proceeded to the next target name (see Figure 3- The Experiment).

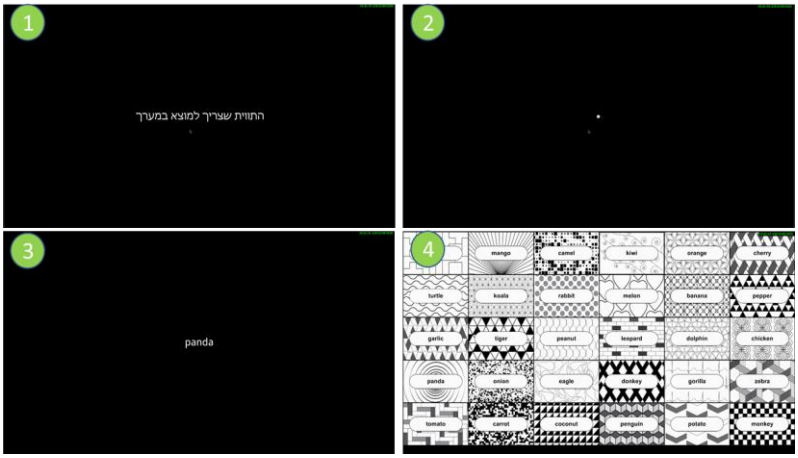


Figure 3- The Experiment

Analysis

Experimental data that were collected through OpenSesame were exported to an Excel file. It detailed each stage of the experiment being tested: label name, background type, high/low spatial frequency, the time it took to select and click the selected label from the visual array, the target label, the label clicked, and whether the participant succeeded in the task. For each participant, we obtained a 30-line file with each line showing the label they were asked to find.

The Tobii Pro Lab eye tracking software was used to identify the user's visual search patterns. This software displayed the values through an Excel file with the following variables: duration of focus on all labels, the number of fixations, and the fixation order. We analyzed this data to identify the elements that influenced participants' visual scanning patterns.

The two files were then consolidated, and the file was used to test the hypotheses. The first two hypotheses were analyzed using R software that allowed a survival analysis model and a GLMM model on the variables to be run. The third hypothesis was tested through an Excel t-test, which examined the significance of the differences between the two groups by comparing the means and analyzing the variance to examine the effect of the independent variables**.**

4. Findings

Response time

Figure 4 presents the median response time in milliseconds (ms) in each condition - the median response time of low spatial frequency labels (2,332 ms) was the shorter than high/low spatial frequency (3,064 ms) and white labels (3,869 ms) (see Figure 4).

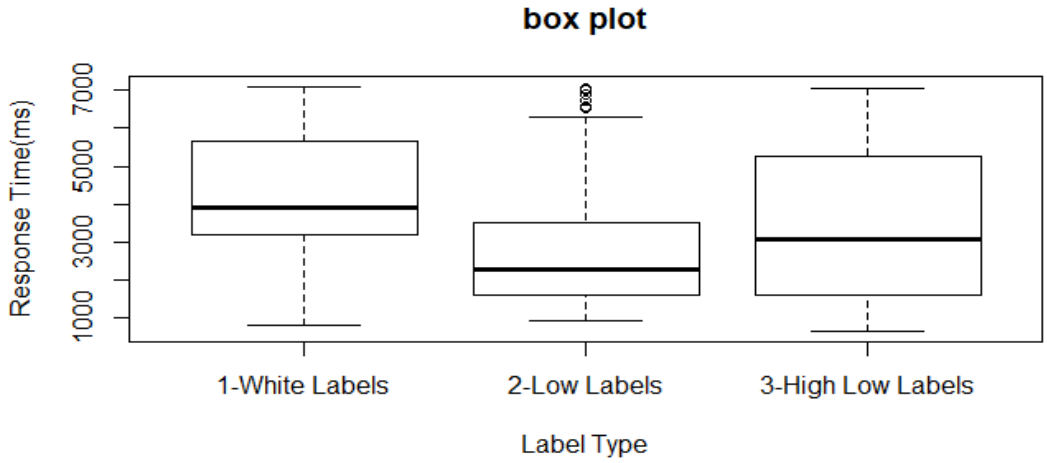


Figure 4 - Box Plot

Additionally, Figure 5 shows the average response times for each condition. The average response time of patterned labels was 2,810.96 and 3,477.62 ms with Sd 1,655 and 2,212.5 for low and high frequency labels respectively. The average response time for the white labels was 4,253 ms with Sd 1,814. The difference between the white condition and low spatial frequency and high–low spatial frequency was significant. The significance level was 6.7E-41 and 1.2E-10 (<0.05). Low spatial frequency labels were those with the shortest average response time (2,810.96 ms) with Sd 1,655, while high–low spatial frequency labels took 3,477.62 ms with Sd 2,212.5. The difference between the low and high–low spatial frequency was significant with a significance level of 4.5E-09 (p<0.05).

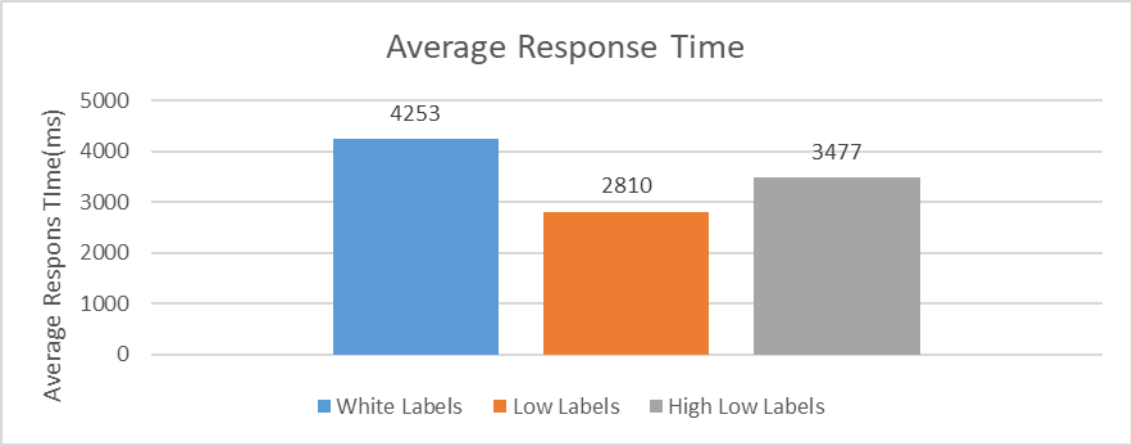


Figure 5- Average Response Time (ms)

The hypothesis was tested using survival analysis and a frailty model (Wienke, 2010). Survival data is a term used for describing data that measure the time to a given event of interest. In survival analysis, the event may be death, occurrence of disease (or complication), time to an epileptic seizure, time it takes for a patient to respond to a therapy, or time from response until disease relapse. Time to an event is a positive real value variable having a continuous distribution. It is necessary to define the starting time point, say 0, from which times are measured. When we measure the length of time for

detection, the starting time is the beginning of the task until the occurrence of the error or correct identification is made (Hanagal, 2011).
In a frailty model, it is necessary to include explanatory variables. The reason is that frailty describes the influence of common unknown factors. If some common covariates are included in the model, the variation owing to unknown covariates should be reduced. Common covariates are standard for all members of the group (Hanagal, 2011). A frailty model is a random-effects model for time variables, where the random effect (the frailty) has a multiplicative effect on the hazard. It can be used for univariate (independent) failure times. The concept of frailty provides a suitable way to introduce random effects in a model to account for association and unobserved heterogeneity. In its simplest form, frailty is an unobserved random factor that modifies multiplicatively the hazard function of an individual or a cluster of individuals (Wintrebert et al., 2007).
From the survival analysis of the response time variable with the other variables, it emerged that the model was influenced by the significance of the label type ($p=0.0039<0.05$) and the experimental phase ($p=2.1E-09<0.05$). As the stage of the experiment progresses, time decreases (meaning that the second game took longer than the experiment). The label type received a positive and significant coefficient indicating a difference between the label types - low spatial frequency labels had the shortest response time, and the white labels had the longest response time.

Response accuracy

The second hypothesis is that the type of label affects the response accuracy. From the data, we obtained the response accuracy variable in the following manner: 0=an incorrect response, not the same as the target label; 1=the correct response at a time between 0 and 7 seconds; and 2=not detectable within 7 seconds. In Figure 6, which shows the distribution of response accuracy in each condition, greater response accuracy in the patterned labels condition (85.7% low labels and 81.8% high –low labels) compared to the white label condition (76.5%). The difference between the two conditions, high–low labels and low labels, with white labels was significant, with a significance level 0.026 and 6.8E-05 ($p<0.05$). The difference between the high–low labels and low labels was not significant 0.072 ($p>0.05$). The low spatial frequency labels had the highest accuracy, 85.7% compared to high spatial frequency 81.8%, and white labels (76.5%) (see Figure 6).

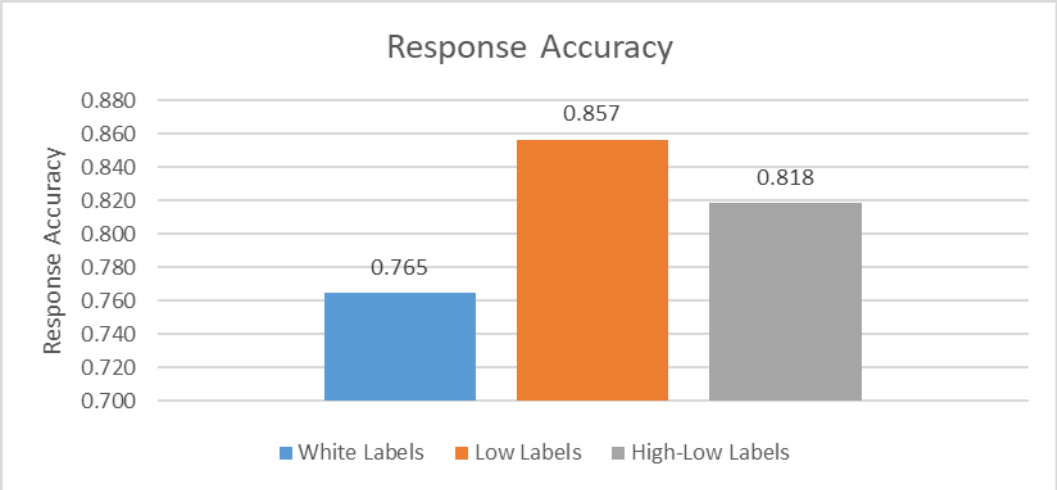


Figure 6-The Percentage of Response Accuracy

The labels with low spatial frequency were those with the highest accuracy and the difference between this label type and the other types was significant. The difference between high spatial frequency labels versus white labels was not significant.
We had more than two levels: in the first level, the participant did not identify the label correctly; in the second level, the participant correctly identified the label; and in the third level, the participant could not identify the label in less than seven seconds. Therefore, we chose to use a multinomial regression, which is an extension of the logistic regression in which the dependent gets more than two levels. Multinomial logit random effects models are a special case of a multivariate generalized linear mixed model (Tutz & Hennevogl, 1996), denoted by MGLMM. This formulation is advantageous for several reasons. As with GLMMs, MGLMMs provide a common framework using a unified notation and estimation method for a broad class of models, including known formulas for score functions and information matrices. A generalized linear mixed model (GLMM) is an extension to the generalized linear model (GLM) in which the linear predictor contains random effects in addition to the usual fixed effects (Breslow & Clayton, 1993; Jiang, 2007; McCulloch & Neuhaus, 2005). GLMMs provide a broad range of models for the analysis of grouped data since the differences between groups can be modeled as a random effect.
From the analysis we found that the label type ($p<0.05$) affected the accuracy of the response so that the coefficient of the label type was positive and the accuracy increased as it moved between the different conditions of the experiment. The label with low spatial frequency had the highest accuracy label.

Eye movement

From the eye movement tracking data, we obtained the fixation on each label that allowed us to analyze the scan pattern and movements between the fixations on both types of labels. We defined three types for switching between two fixations (vertical, transverse, diagonal). Therefore, we were able to plot the movement between each fixation, and examine whether the way of scanning was different for the label types.
We transformed the fixation location coordinates by screen pixels (1920 x 1050), so that each label was 320 x 200 pixels in size. The top label on the left was the first label (0–320, 0–200). The difference between two fixation positions allowed us to count the number of movements from one label to another on both the X and Y axes.
After arranging the data according to the scanning pattern, we calculated the number of movements on each of the axes when searching for each type of labels. We did a t-test to compare between the two types of labels.
After arranging the data of the eye movement system, with white background labels, there were 14.9 fixations. Out of these, there was 4.06 diagonal movements and 10.9 X–Y axis movements. In low spatial frequency labels, there were 10.23 fixations, of which there were 3.41 diagonal and 6.81 X–Y axis movements. In high–low spatial frequency labels, there were 12.3 fixations, of which, 4 were diagonal and 8.1 were X–Y axis movements.
From the t-test, the average percentage of diagonal fixations on white labels was 0.278, on high–low labels 0.347, and on low labels 0.34. There was a difference in the search method between the two types of labels (high–low labels and low labels) with white labels, and this difference was significant (2.15E-09 and 1.43E-07<0.05), rejecting the hypothesis that the two types were similar. The patterned labels appear to have had an unordered scanning method.

5. Discussion and Conclusions

The labels with white background resulted in longer response times and lower accuracy compared to those with patterns. These findings confirmed Hypothesis 1a. Similarly, in Hypothesis 1b, the results demonstrate that participants could identify labels with low spatial frequency faster than those with high spatial frequency. The background label condition was faster than the white background condition, and the low spatial frequency labels also showed an improvement in the response times compare to the response times of high spatial frequency labels.

In relation to Hypothesis 2, the accuracy for labels with patterns was higher than accuracy for labels with a white background. This indicates that the participants were assisting in the design of the visual search task. Adding patterns seemed to increase the accuracy of the responses that occurred. While the white background condition accuracy was 0.746, the label mode with the pattern experienced a percentage of 0.805 accuracy with a statistically significant difference in response accuracy. Therefore, there is an improvement in the accuracy of the identification. In addition, labels with a low spatial frequency pattern had the highest accuracy relative to labels with high spatial frequency patterns.

In relation to Hypothesis 3, the average percentage of diagonal fixations on labels with patterns was higher than percentage for labels with a white background. This indicates that the characteristics of visual patterns affect the visual scanning method. The patterns allowed participants to search more efficiently.

The low frequency group tended to provide the shortest response times, and these times tended to increase along with the dominant spatial frequency to a point. So predictable features in patterns with lower dominant spatial frequency may be more distinct, allowing easier identification and faster response times.

A possible explanation for these results is that dominant spatial frequency patterns with more distinguishable features potentially allow a guided search. However, beyond a certain higher spatial frequency level, the features become less distinguishable and can no longer be guided, and a full self-termination of the patterns must be performed. This would explain why the low frequency group demonstrated the lowest response times.

Similar to the response time results, the low dominant spatial frequency group exhibited the highest accuracy rate and was higher than that observed in the high dominant spatial frequency group. That is, at low frequencies, pattern features tend to be more noticeable, allowing for easier and more accurate responses. As the dominant spatial frequency increases these features become more difficult to discern and, thus, identification of the correct label becomes more difficult and errors occur. Combined, the response time results and accuracy rates presented above suggest that spatial frequency influences identification.

In the third hypothesis, we hypothesized that the characteristics of visual patterns would impact the method of visual scanning. The results show that white labels have a more orderly crawl that is scanned by columns or rows, whereas labels with a design are different and unordered. It may be due to spatial frequency that allows some of the labels to be more prominent and causing the eye to focus more on some of the labels. From this result, these backgrounds can be used to design high-demand medications, which can reduce search times.

Limitations and Future Research

Corona virus (COVID-19) led to a limitation in recruiting participants so that we could not recruit participants from other population such as pharmacists and elderly participants. Therefore, we decided to run the experiment on students and using label names that students were familiar with such as fruit, vegetable, and animal names instead of drug names.

Conclusion

Medication errors are a complicated issue; by definition, a wide variety of actions/inactions constitute medication errors. Therefore, efforts to determine the incidence of medication errors should also consider a wide range of actions. The prevalence estimates are further complicated by the different methods used to collect and quantify the error reports. As a result, estimates of the extent of the problem are diverse and debatable. What cannot be debated is that medication errors do occur in most, if not all, medical fields. Of course, medication errors can have a significant and lasting negative impact on patients' health outcomes. While education and training can help mitigate rule-based knowledge and mistakes, errors characterized by slips and lapses are more appropriate for prevention through systemic solutions.

In this study, the advantage of using visual patterns in labeling can be seen as an empirically tested alternative to enhancing or assisting in medication identification. Human abilities with respect to texture/pattern perception were considered for designing an array of visual patterns that would be used to help identify simulated labels. However, the results of the experiment showed that adding a pattern to the background labeling space significantly improved the detection speed, compare to the response to white background label mode. In addition, response accuracy was higher for low spatial frequency labels compared to white background labels. Therefore, the results of this study may help create the basics of using templates as a tool to improve medication identification.

6. Policy Implications and Recommendations

The need for a standard medication labeling is clear, and there is no doubt that it will reduce the number of medication errors. The use of visual patterns as background that were evaluated in this study present promising potential for a new approach in improving medication identification. Our recommendations suggest that policy makers should consider the use of such solution as part of future standard for medication labeling.

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