Chapter 80

Attentional Biases for Betel Nut Cues

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**Abbreviations**

- **ABM** Attentinal bias modification
- **DSM-IV** Diagnostic and Statistical Manual of Mental Disorders IV
- **IARC** The International Agency for Research on Cancer
- **ICD-10** International Classification of Diseases 10
- **STM** Short-term memory

**BETEL NUT: EASTERN DELICACY, WESTERN CARCINOGEN**

Dissolve flatulence and phlegm, ease hangover, facilitate digestion, eliminate toxins from overindulgence of fat and sweet foods, gourmet for everyone to enjoy.

S. H. Wang (1861)

Many more studies now provide evidence for the carcinogenicity of betel quid without tobacco for oral cancer and for betel quid with tobacco for cancers of the oral cavity, pharynx and oesophagus.

IARC (2004)

A betel nut (also called betel quid) usually consists of three major ingredients: a raw areca nut, slaked lime, and *Piper betle* inflorescence. The size of a betel nut is usually about 3 cm × 3 cm × 2 cm (Figure 1). The acidity of a raw areca nut can cause stomach problems after repeated intake. With high alkalinity, the slaked lime can neutralize this acidity. Arecoline (the primary alkaloid in raw areca nut) has been shown to act on the muscarinic and nicotinic acetylcholine receptors (Chu, 2001) and affect various cognitive functions (e.g., attention and memory) (Freo, Pizzolato, Dam, Ori, & Battistin, 2002; Ho & Wang, 2010, 2011).

Back in the late nineteenth to early twentieth centuries, betel nut was popular among the nobles and the wealthy in Chinese society (S. Q. Wang, 1999). They would carry the small, delicate betel-quid bags (or boxes) with them and give betel nuts as presents on social occasions. Early Chinese medicine books and cookbooks declared great benefits from chewing betel nut. For example, chewing betel nut can facilitate digestion and ease hangover (S. H. Wang, 1861). In early Taiwan, the spiritualists in some aboriginal tribes would cast spells on the raw areca nuts, which were believed to represent human bodies in these tribes. However, during the Japanese colonial period (1895–1945), the use of betel nut was strictly prohibited.

In the late twentieth century, when the betel nut was subjected to modern Western addiction theory and methodology, the dark side of the betel nut was gradually revealed. On the notorious dark side are the probable dependence symptoms betel nut chewers may develop in terms of Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) and International Classification of Diseases 10 (ICD-10) criteria (Benegal, Rajkumar, & Muralidharan, 2008; IARC, 2004; Lee et al., 2014; Li, Ho, Tang, & Chang, 2012; Winstock, 2002). Moreover, the chemical ingredients in a raw areca nut such as arecoline (the major alkaloid) and polyphenols have been identified as chemical carcinogens (IARC, 2004).

In this chapter, we selectively review the literature regarding attentional biases in addictive behaviors in general and in betel nut chewers in particular. Attentional bias toward substance cues is an important issue in addiction development; it has been reported to be related to subjective craving (Field, Munafò, & Franken, 2009), impulsivity (Coskunpinar & Cyders, 2013), and treatment outcomes (Cox, Hogan, Kristian, & Race, 2002; Marissen et al., 2006). Lastly, we delineate a cognitive neuroscience approach to investigate various unexplored issues related to betel nut chewers, such as short-term memory (STM). Studies on these unexplored issues can facilitate our understanding of betel nut chewing. More effective treatments can be developed accordingly.

**ATTENTIONAL BIASES IN ADDICTIVE BEHAVIORS**

In the literature on cognitive neuroscience, how people deploy their attention in surroundings full of information has been extensively studied. Since human processing capacity is presumably limited, selection is crucial to prevent overloading our cognitive processes with unnecessary information. Extensive studies on attention and cognition describe attentional selection as driven by both top-down factors (e.g., history of being rewarded) and bottom-up factors (e.g., physical salience) (Awh, Belopolsky, & Theeuws, 2012; Desimone & Duncan, 1995; Nakayama & Martini, 2011).
Works on the effect of reward history (one of the top-down factors) of attentional selection (Pessoa & Engelmann, 2010) have demonstrated that commitment to the pursuit of a goal (e.g., extrinsic and/or intrinsic rewards) makes individuals selectively attend to cues associated with those goals at the cost of other cues. This biased attention can prioritize the associated cues through various brain regions involved in emotional and cognitive processes (Desimone & Duncan, 1995). Links between reward and attention are suggested to be implemented by brain areas involved in both dopaminergic responses (e.g., lateral intraparietal sulcus and anterior cingulate cortex), point-to-point interactions (e.g., orbital frontal cortex projecting to ventral lateral prefrontal cortex), or subcortical dopaminergic projections (e.g., ventral tegmental area and nucleus accumbens, NAcc) to widespread cortical areas (Pessoa & Engelmann, 2010).

Addictive substances have long been considered as reinforcers that can shape the users’ behaviors and brains (Koob & Volkow, 2010; Robinson & Berridge, 2003; Solomon & Corbit, 1974). Hedonic states brought about by addictive substances can increase the probability of impulsive substance use (i.e., positive reinforcement) (Koob & Volkow, 2010), enhancing incentive motivational values of these substances by sensitizing relevant brain areas (e.g., NAcc) (Robinson & Berridge, 2001, 2003). Removal of subsequent opponent, unpleasant states due to withdrawal of substances (Solomon & Corbit, 1974) increases the probability of compulsive substance use (i.e., negative reinforcement) (Koob & Volkow, 2010), influencing the activation of extended amygdala (Seo & Sinha, 2011).

Top-down reward-driven attentional selection has been repeatedly observed in the field of substance use and abuse (Coskunpinar & Cyders, 2013; Field & Cox, 2008; Field et al., 2009; Robbins & Ehrman, 2004). Field and Cox (2008) provide a great review on biased attention toward substance cues. Numerous studies report that the substance users of alcohol, nicotine, opiates, cocaine, cannabis, and so on, rather than the nonusers, exhibited biased attention toward the substances they often use. Studying attentional bias is important, because attentional bias toward substance cues has been reported in association with critical psychological and cognitive factors in addiction. For example, a meta-analytic study (Field et al., 2009) indicated a significant correlation ($r=0.19$) between attentional bias and self-reported craving. This elevated craving can increase the probability of substance use behaviors (Kavanagh, Andrade, & May, 2005; Schoenmakers et al., 2010). Impaired executive cognitive functions and impulsivity in substance users (Ersche et al., 2012; Heatherton & Wagner, 2011) may be related to attentional bias (Coskunpinar & Cyders, 2013; Fadardi & Cox, 2006). Another meta-analytic study (Coskunpinar & Cyders, 2013) reported a significant correlation ($r=0.20$) between impulsivity and attentional bias. Attentional bias can predict relapse after treatment (Cox et al., 2002; Marissen et al., 2006).
The visual probe task is a commonly employed task to measure attentional bias toward substance cues. In a typical visual probe task (Figure 2), participants are required to respond as quickly as possible to a visual probe (e.g., an arrow directing upwards or downwards) presented immediately after the offset of a pair of substance-related stimuli (pictures or words). Critically, one of the stimuli is related to the addictive substance. Many studies (Coskunpinar & Cyders, 2013; Field & Cox, 2008; Littel, Euser, Munafo, & Franken, 2013; Robbins & Ehrman, 2004) have reported that substance users responded faster to the probe replacing a substance-related stimulus than to a matched, unrelated one. This indicates a preferential attentional allocation to the locations of substance-related stimuli (i.e., attentional bias toward substance cue).

The presentation duration of a pair of substance-related stimuli can be manipulated to investigate different phases of attentional processing. To investigate preconscious attentional bias, the presentation duration is set under the awareness threshold (e.g., 17 ms). In this extremely brief presentation, a backward mask (usually in a mosaic format) is implanted to avoid visual persistence. This can ensure the exact presentation. An awareness check is adopted to check whether stimuli remain in the subliminal processing. However, previous studies (Ho, Chang, Li, & Tang, 2013; Mogg, Bradley, Hyare, & Lee, 1998) employing the appetitive cues usually did not report subliminal attentional biases.

On the other hand, relatively longer presentation durations (e.g., 200–2000 ms) are adopted to investigate supraliminal attentional bias. Rapid presentations (e.g., 200 ms or shorter) may reflect initial attentional orienting, possibly involving single eye movements to the cue given, so that saccades can be initiated within as little as 120–130 ms (Crouzet, Kirchner, & Thorpe, 2010). Longer presentations (e.g., 2000 ms) allow multiple eye movements based on the cues (Wright & Ward, 2008), representing maintained attention (Franken, 2003). Some studies (Mogg & Bradley, 2002; Robbins & Ehrman, 2004) adopted 500-ms presentation duration. These studies consider this duration to reflect initial attentional orienting. However, this duration may have allowed multiple eye movements (Crouzet et al., 2010), possibly representing maintained attention.

Positive reinforcing models (Robinson & Berridge, 1993, 2000, 2001, 2003) and negative reinforcing models (Baker, Brandon, & Chassin, 2004; Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Solomon & Corbit, 1974) have been proposed to account for attentional bias toward substance cues. Note that these two types of models are not mutually exclusive. The incentive-sensitization model (Robinson & Berridge, 1993, 2000, 2001, 2003) may be the best known positive reinforcing model. This model proposes that repeated administration of addictive substances can render the brain hypersensitive to these substances and related cues (i.e., the conditioned stimuli, CS), i.e., the brain (particularly the NAcc-related circuits) (Koob & Volkow, 2010) becomes enduringly hypersensitive or sensitized to the substance and the CS. This sensitization may involve changes in neurochemistry in the NAcc-related circuits (e.g., an increase in dopamine and glutamate, and in the length and density of dendrites in the NAcc) potentiating the related neural pathways (e.g., the mesolimbic dopamine pathway) (Robinson & Berridge, 2003). This sensitized brain and subsequently enhanced incentive value of substance can “grab” the addicts’ attention (i.e., attentional bias).

The negative reinforcing models (Baker, Brandon, et al., 2004; Baker, Piper, et al., 2004; Solomon & Corbit, 1974) suggest that in order to alleviate or avoid negative states (e.g., distress) induced by substance withdrawal, compulsive substance-seeking behaviors are initiated and maintained. The compulsive-seeking behavior continues in spite of a “blunt” reward value, heightened negative mood and stress sensitivity the substances elicit (Seo & Sinha, 2011). The preconscious detection of the above-mentioned negative signals inflates the incentive values of substances, thereby

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1. Another common task is the addiction Stroop task (Cox, Fadardi, & Pothos, 2006). In this task, participants are required to respond as quickly as possible to the color of the ink in which a series of words or pictures are printed. For dependent participants, color-naming reaction times are significantly slower when the words or pictures are related to the substance they are addicted to. Attentional biases measured in the addiction Stroop task and the visual probe task may reflect different aspects of attention. The visual probe task may reflect attentional biases “in a spotlight scanning different aspects of the visual field” (Mogg et al., 2000); whereas the addiction Stroop task where the cue is usually visible until response may reflect attentional biases “in an isolated spotlight of attention” (Mogg et al., 2000). In this chapter, we primarily focus on the visual probe task.

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**FIGURE 2** *Example procedure of visual probe task.* A pair of pictures presented for 17 ms, 200 ms, or 2000 ms. Note that in the 17-ms condition, a backward mask is adopted to prevent visual persistence.
basing attention toward them (Baker, Piper, et al., 2004). The interplay between negative states and inflated incentive values may be implemented by the interactions between the amygdala–striatum reward system (e.g., the decreased activation of the extended amygdala and the striatum due to chronic substance use) and the prefrontal control system (e.g., the dysfunctional orbital frontal cortex and ventral lateral prefrontal cortex) (Baker, Piper, et al., 2004; Seo & Sinha, 2011).

Imaging and electrophysiological studies (Janes et al., 2010; Kang et al., 2012; Littel et al., 2012; Luijten et al., 2011) report that attentional bias toward the addictive substance involves brain areas associated with reward and attentional systems. For example, the presence of smoking cues results in activation of the reward system (e.g., the insula and the dorsolateral prefrontal cortex) and the attentional system (e.g., the posterior cingulate cortex, the anterior cingulate cortex, and the superior parietal gyrus) (Kang et al., 2012). Moreover, attentional bias measured by the eye tracker was positively correlated with activations of various brain areas involved in reward (e.g., the dorsolateral prefrontal cortex) and attention (e.g., the posterior cingulate cortex) (Kang et al., 2012). A meta-analytic study on electrophysiological indices (Littel et al., 2012) reported that the late event-related potentials components, such as P300 (300–800 ms after stimulus onset) and slow potential (>800 ms after stimulus onset), reflect a top-down, motivated attentional processing of the substance cues. These substance-elected components can be observed in the frontal and parietal electrode sites that are involved in both reward and attention, as reported in the imaging literature (Koob & Volkow, 2010; Pessoa & Engellmann, 2010).

Attentional bias toward substance cues may be reduced using attentional bias modification (ABM) (Schoenmakers et al., 2010). Many studies employ the attentional retraining procedure developed by MacLeod et al. (2002) in anxious participants. This procedure is similar to that of the typical visual probe task mentioned above, except for the probe location. In the training session, after a pair of substance-related stimuli disappears, a probe consistently appears at the location previously occupied by the substance-free stimulus (e.g., a smoking-free picture). The probe in the training session is presumed to divert the trainees’ attention from the substance-related stimulus (e.g., a picture of smoking). Although this modified visual probe task can reduce the attentional bias toward substances, a meta-analytic study (Mogoșe et al., 2014) provided evidence that the ABM for addictive behaviors may not be as effective as that for anxiety. Possibly, ABM alone may be insufficient for initiating a change in appetitive motivation. Training programs to enhance the general control ability may also be required (Klingberg, 2010; Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013).

**ATTENTIONAL BIASES FOR BETEL NUT CUES**

Ho et al. (2013) examined whether the habitual betel nut chewers can exhibit attentional biases toward the betel nut cues. It is pioneering work in adopting a cognitive task (i.e., the visual probe task) in the study of betel nut addiction in Asian countries, where betel nut is a commonly used substance. This study can shed some light on understanding the chewers’ cognition and pave a way to develop abstinence treatment.

Ho et al. (2013) employed the modified visual probe task to assess the habitual betel nut chewers’ attention bias toward betel nut cues. This task was similar to a study done by Bradley, Field, Mogg, and De Houwer (2004). In Ho et al. (2013), betel nut pictures were used; each betel nut picture was presented alongside its matched betel nut-free picture. The presentation durations of pairs of pictures were 17 ms, 200 ms, and 2000 ms. After the offset of pictures, a probe (an upward or downward arrow) appeared on either the betel nut picture or the matched picture. Participants were instructed to respond to the direction of the arrow as quickly as possible. Degree of dependency was measured via the Betel Nut Dependency Scale (BNDS) (Li et al., 2012). The BNDS is composed of three factors: “desire” (four items), “withdrawal reaction” (four items), and “habit of using” (three items). Each item could be rated from one (“totally disagree”) to four (“totally agree”). Total scale score ranged from 11 to 44, with 24 as the cutoff point. Besides the difference in dependency, the heavily dependent and lightly dependent groups still differed in: weekly expense on betel nut, daily consumption, urge, and hours since the last chewing (Table 1). Age and monthly income did not show significant difference between the two groups.

Ho et al. (2013) found that when the presentation duration was 200 ms and 2000 ms, heavy chewers had a shorter reaction time than light chewers in responding to the probe replacing the betel nut pictures (Table 2). This indicated that heavy chewers exhibited attentional biases toward the betel nut cues. More specifically, heavy chewers showed the initial orienting (200 ms) and maintained attentional (2000 ms) bias toward betel nut cues. However, when the pictures were flashed shorter than the awareness threshold (17 ms), neither group exhibited such attentional bias. Correlation analysis was adopted to examine relationships between attention bias (overall and at three durations) and betel nut measurements in Table 1 (Table 3). Ho et al. reported that attentional bias was positively related to many betel nut measurements such as degree of dependency, urge to chew, and weekly expense.

The finding of initial orienting toward substance may depend on the substance used. For instance, this attentional bias was found in a nicotine study (Bradley et al., 2004), but not in an alcohol study (Field, Mogg, Zetteler, & Bradley, 2004). This difference in attentional bias could be due to the various degrees of incentive salience resulting from different substances. Betel nut or cigarette might result in incentive salience faster than alcohol. Betel nut or cigarette might gain incentive salience faster than alcohol. Betel nut or cigarette might gain incentive salience faster than alcohol. Thus, attention could be captured even within a very short time. In contrast, maintained attention (2000 ms) has been consistently observed across various substances. Heavy betel nut chewers may be more motivated to consume betel nuts, thereby causing such bias (LaBerge, 1995). Lastly, Ho et al. (2013) did not observe subliminal attentional biases (17 ms) toward betel nut cues. A possible explanation is that the occurrence of subliminal attentional bias varies across stimuli. Some studies find that such subliminal attentional biases may be more likely to appear in aversive stimuli, such as angry faces (Cisler, Bacon, & Williams, 2009) than in appetitive stimuli (Bradley et al., 2004; Weinstein & Cox, 2006). More studies are required to test this hypothesis.

2. In addition to the most popular modified visual probe, there are other tasks modified to train attention such as the spatial cuing task and the visual search task. Please refer to Mogoșe et al. (2014) for a review.
### TABLE 1 Characteristics of Heavy and Light Betel Nut Chewers

<table>
<thead>
<tr>
<th></th>
<th>Heavy Chewers (N = 53)</th>
<th>Light Chewers (N = 42)</th>
<th>t(93)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNDS</td>
<td>30.4 (3.8)</td>
<td>20.7 (3.7)</td>
<td>12.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.1 (9.1)</td>
<td>28.9 (9.3)</td>
<td>0.6</td>
<td>n.s.</td>
</tr>
<tr>
<td>Monthly income</td>
<td>2.4 (1.1)</td>
<td>2.3 (1.3)</td>
<td>0.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>Weekly expense</td>
<td>4.7 (1.9)</td>
<td>3.9 (1.8)</td>
<td>2.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Number per day</td>
<td>27.6 (29.2)</td>
<td>15.4 (11.4)</td>
<td>2.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Days per week</td>
<td>5.0 (1.9)</td>
<td>4.0 (1.9)</td>
<td>2.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Months</td>
<td>93.9 (93.7)</td>
<td>66.6 (80.2)</td>
<td>1.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>Urge to chew (pretask)</td>
<td>6.1 (1.9)</td>
<td>3.2 (1.9)</td>
<td>7.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urge to chew (middle task)</td>
<td>6.2 (2.2)</td>
<td>3.1 (2.2)</td>
<td>6.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urge to chew (posttask)</td>
<td>6.3 (2.3)</td>
<td>3.5 (2.6)</td>
<td>5.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hours since last chew</td>
<td>7.2 (14.2)</td>
<td>17.1 (25.2)</td>
<td>2.5</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Standard deviations are in parentheses. For the weekly expense, participants selected from the following options (unit is the New Taiwan dollar): (1) none, (2) within 100, (3) 100–200, (4) 200–300, (5) 300–400, (6) 400–500, and (7) over 500. For monthly income, participants selected from the following options (unit is thousands of New Taiwan dollars): (1) lower than 10, (2) 10–20, (3) 20–30, (4) 30–50, (5) over 50.

BNDS, Betel Nut Dependency Scale; n.s., non-significant.

Data from Ho et al. (2013) and Tang (2013). Reprinted with permission from the American Psychological Association.

### TABLE 2 Mean Reaction Times and Standard Errors of Means (in Parentheses) in Three Presentation Durations

<table>
<thead>
<tr>
<th></th>
<th>Heavy Chewers (N = 53)</th>
<th>Light Chewers (N = 42)</th>
<th>t(52)</th>
<th>p</th>
<th>t(41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matched Betel Nut Bias</td>
<td>Matched Betel Nut Bias</td>
<td>Matched Betel Nut Bias</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 ms</td>
<td>550.2 (14.9)</td>
<td>550.3 (15.6)</td>
<td>−0.1</td>
<td>0.03</td>
<td>531.8 (16.7)</td>
<td>533.0 (17.5)</td>
</tr>
<tr>
<td>200 ms</td>
<td>653.2 (17.0)</td>
<td>628.4 (15.2)</td>
<td>24.8</td>
<td>3.1</td>
<td>&lt;0.005</td>
<td>596.7 (19.1)</td>
</tr>
<tr>
<td>2000 ms</td>
<td>657.9 (16.7)</td>
<td>632.8 (14.4)</td>
<td>25.1</td>
<td>1.9</td>
<td>0.06</td>
<td>604.3 (18.8)</td>
</tr>
<tr>
<td>Average</td>
<td>620.5 (15.1)</td>
<td>603.8 (14.0)</td>
<td>16.7</td>
<td>2.4</td>
<td>&lt;0.05</td>
<td>577.6 (17.0)</td>
</tr>
</tbody>
</table>

Heavy chewers exhibited attentional biases toward the betel nut cues at 200 ms and 2000 ms durations. n.s., non-significant.

Data from Ho et al. (2013) and Tang (2013). Reprinted with permission from the American Psychological Association.
### TABLE 3 Correlations Between Attentional Bias and Betel-Related Measures

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>0. Overall bias</td>
<td>0.33**</td>
<td>0.79**</td>
<td>0.92**</td>
<td>-0.05</td>
<td>0.05</td>
<td>0.24*</td>
<td>0.05</td>
<td>0.24*</td>
<td>0.00</td>
<td>0.30**</td>
<td>0.23*</td>
<td>0.21*</td>
<td>0.26**</td>
<td>-0.13</td>
</tr>
<tr>
<td>1. Bias at 17 ms</td>
<td>-</td>
<td>-0.00</td>
<td>0.16</td>
<td>-0.04</td>
<td>0.14</td>
<td>0.14</td>
<td>0.09</td>
<td>0.04</td>
<td>-0.07</td>
<td>0.11</td>
<td>0.12</td>
<td>0.06</td>
<td>0.06</td>
<td>0.01</td>
</tr>
<tr>
<td>2. Bias at 200 ms</td>
<td>-</td>
<td>0.58**</td>
<td>0.02</td>
<td>0.09</td>
<td>0.23*</td>
<td>-0.07</td>
<td>0.24*</td>
<td>0.07</td>
<td>0.26*</td>
<td>0.17</td>
<td>0.16</td>
<td>0.24*</td>
<td>-0.13</td>
<td></td>
</tr>
<tr>
<td>3. Bias at 2000 ms</td>
<td>-</td>
<td>0.08</td>
<td>-0.04</td>
<td>0.18</td>
<td>0.10</td>
<td>0.20</td>
<td>-0.01</td>
<td>0.26*</td>
<td>0.21*</td>
<td>0.21*</td>
<td>0.23*</td>
<td>0.23*</td>
<td>-0.12</td>
<td></td>
</tr>
<tr>
<td>4. Age</td>
<td>-</td>
<td>0.45*</td>
<td>0.43**</td>
<td>0.26*</td>
<td>0.42**</td>
<td>0.60**</td>
<td>0.10</td>
<td>-0.03</td>
<td>0.01</td>
<td>0.03</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Monthly income</td>
<td>-</td>
<td>0.42**</td>
<td>0.25*</td>
<td>0.42**</td>
<td>0.44**</td>
<td>0.15</td>
<td>-0.04</td>
<td>0.08</td>
<td>0.04</td>
<td>-0.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Weekly expense</td>
<td>-</td>
<td>0.46**</td>
<td>0.67**</td>
<td>0.48**</td>
<td>0.32**</td>
<td>0.27**</td>
<td>0.33**</td>
<td>0.24*</td>
<td>-0.20*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Number per day</td>
<td>-</td>
<td>0.43**</td>
<td>0.41**</td>
<td>0.29**</td>
<td>0.23*</td>
<td>0.42**</td>
<td>0.18</td>
<td>-0.20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Days per week</td>
<td>-</td>
<td>0.45**</td>
<td>0.33**</td>
<td>0.31**</td>
<td>0.39**</td>
<td>0.28**</td>
<td>-0.34**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Months</td>
<td>-</td>
<td>0.23*</td>
<td>0.13</td>
<td>0.30**</td>
<td>0.20</td>
<td>-0.16</td>
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<tr>
<td>10. BNDS</td>
<td>-</td>
<td>0.58**</td>
<td>0.55**</td>
<td>0.49**</td>
<td>-0.35**</td>
<td></td>
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<tr>
<td>11. Urge to chew (pretask)</td>
<td>-</td>
<td>-</td>
<td>0.83**</td>
<td>0.77**</td>
<td>-0.14</td>
<td></td>
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<tr>
<td>12. Urge to chew (middle task)</td>
<td>-</td>
<td>-</td>
<td>0.75**</td>
<td>-0.13</td>
<td></td>
<td></td>
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<tr>
<td>13. Urge to chew (posttask)</td>
<td>-</td>
<td>-</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
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<td>14. Hours since last chew</td>
<td>-</td>
<td>-</td>
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</table>

Overall bias, bias at 200 ms, and bias at 2000 ms are correlated with many betel-related measurements listed in Table 1.

* p<0.05; ** p<0.001.

*BNDS, Betel Nut Dependency Scale.*

Data from Ho et al. (2013) and Tang (2013). Reprinted with permission from the American Psychological Association.
Shen and Ho (2014) examined betel nut chewers’ eye movement patterns on the betel nut cues when these cues are presented for a longer duration (e.g., 2000 ms) (Shen & Ho, 2014). Eye-tracking technology directly measures visual attention by recording where participants direct their gaze. This method enables us to obtain higher ecological validity than with visual detection tasks alone (Marks et al., 2014; Miller & Fillmore, 2011). Shen and Ho adopted the same experimental materials as Ho et al. (2013), with only a slight change in experimental procedure. Presentation duration was set at 2000 ms to allow for multiple eye movements. An eye-tracking machine recorded two major types of information: probability (or frequency) and time. The probability measures included: (1) the probability of initial fixation and (2) the number of fixations. The time measures included: (1) the latency of initial fixation, (2) the duration of initial fixation, and (3) the gaze duration of total fixations. These measures compared the betel nut cues and the matched cues (betel nut free). Shen and Ho’s study recruited both betel nut chewers as well as those who had never tried betel nut. The two groups did not show difference in age, monthly income, or gender ratio. They differed only in the chewing experience. The preliminary data showed a higher probability for betel nut chewers’ eyesight to move toward betel nut pictures (Figure 3). They fixated on the betel nut picture for a longer duration and with more fixation points. Extending the finding based on RT (reaction time) at 2000 ms in Ho et al. (2013), Shen and Ho (2014) can further account for the shifting of overt attention between images. This new methodology allows us to obtain more direct evidence on attentional bias, and thus provide previous studies with a more solid ground.

COGNITIVE NEUROSCIENCE IN BETEL NUT STUDY

To summarize, the habitual betel nut chewers can exhibit attentional biases toward betel nut cues. Moreover, these chewers can rapidly orient their attention to the betel nut cues (involving a single eye movement) and maintain their attention (involving multiple eye movements) on them. In addition to this motivated attentional processing to betel nut cues, chewing betel nut per se can have acute and long-term effects on chewers’ cognition. Studies in cognitive neuroscience provide us with effective and reliable measuring tools and theoretical frameworks to assess the acute and long-term chewing effects. Herein, we briefly review a number of studies showing that chewing betel nut can affect attention (Ho, Li, & Tang, 2015; Ho & Wang, 2010, 2011) and memory (Chiu & Ho, 2014).

Ho et al. (2015) examined whether chewing betel nut can affect sustained attention and inhibitory control after sleep deprivation. They observed that chewing betel nut had a chronic benefit on habitual chewers’ sustained attention (but not on inhibitory control). However, chewing betel nut did not have acute effects on sustained attention nor inhibitory control. In another study (Ho & Wang, 2010), Ho and Wang reported that after one night of sleep deprivation, betel nut chewing could immediately broaden the useful field of sight for habitual chewers, but not of the nonchewers. Ho and Wang (2011) distinguish between sensory processing and attentional processing by employing contour masking and object masking. They found that for both chewers and nonchewers, betel nut chewing can acutely affect attentional processing, but not sensory processing. That is, betel nut chewing immediately concentrated the habitual chewers’ and nonchewers’ attention foveally (tunnel vision), but to a lesser extent for the habitual chewers. Chiu and Ho (2014) examined whether chronic betel nut chewing can affect habitual chewers’ STM. They examined three components of STM in particular: spatial (remember spatial locations), verbal (remember digits), and visual (remember novel objects). Their preliminary data suggest that chronic betel nut chewing primarily deteriorates spatial STM.

APPLICATIONS TO OTHER ADDICTIONS AND SUBSTANCE MISUSE

In Taiwan, many betel nut chewers are also cigarette smokers and alcoholic beverage drinkers (Wen et al., 2005). This concurrent use of betel nut, cigarette, and alcohol has been reported to expose these users to a higher risk of cancer(s) (e.g., esophageal cancer and/or oral cancer) (Wu et al., 2006). For example, the concurrent use of these three substances can increase the likelihood of contracting esophageal cancer (Lee et al., 2005). Therefore, we suggest that (at least) in the following discussion about betel nut, the concurrent use of other substances should be considered.

First, when surveying betel nut dependence, the concurrent use of cigarette smoking should be taken into consideration (Ho, 2014). Previous studies have shown that the chewers using the areca nut with tobacco additives have higher probability of meeting the dependence criteria in DSM-IV and ICD-10 relative to the chewers using the areca nut only (Benegal et al., 2008). Due of the concurrent use of betel nut and cigarette and similar neurological mechanisms of both (act on the muscarinic and nicotinic acetylcholine receptors) (Chu, 2002), the cross-substitutability of betel nut (particularly with tobacco additives) and cigarette should be heeded when betel nut dependence is assessed.

Second, when assessing the possible impairments in cognitive functions (e.g., STM) and brain functions or structures owing to betel nut chewing, the concurrent use of other substances (particularly cigarette and alcohol) should be considered. Excessive use of addictive substances can cause abnormalities in brain structure and functional impairment (e.g., inhibitory control) (Ersche, Williams, Robbins, & Bullmore, 2013; Ersche et al., 2012). Therefore, to assess the effect of betel nut chewing on cognitions and brain activities, concurrent usage of cigarette and alcohol should be recorded and controlled.
DEFINITION OF TERMS

Betel nut A well-known stimulant in many Asian countries. A betel nut consists of a raw areca nut and the following optional ingredients: slaked lime, Piper betle, Piper betle leaf, Piper betle inflorescence, and tobacco.

Attentional bias to substance cues A top-down reward-driven attentional selection. Works on effect of reward history of attentional selection have demonstrated that committing to a goal pursuit (e.g., substance use) makes individuals selectively attend to substance cues associated with those goals at the cost of other non-substance cues. This biased attention can prioritize the associated substance cues through various brain regions involved in reward and attention.

Attentional retraining A technique aiming to modify the attentional bias that may be detrimental psychologically and physically (e.g., attentional bias to addictive substances). A typical retraining procedure is to direct attention to the neutral (e.g., substance-free) cues (or divert attention from substance cues).

Eye tracking A technique to monitor and record parameters regarding eye movements such as fixations, saccades, pursuits, and so on.

Dopaminergic pathways Neural pathways that transmit the neurotransmitter dopamine from one brain area to another. The mesolimbic dopamine pathway is one of the dopaminergic pathways and plays a critical role in development of addiction.

Positive reinforcement The hedonic states brought about by addictive substances can increase the probability of impulsive substance use, thereby enhancing incentive motivational values of these substances by sensitizing pertinent brain areas (e.g., NAcc).

Negative reinforcement Removal of subsequent opponent, unpleasant states due to withdrawal of substances increases the probability of compulsive substance use, influencing the activation of extended amygdala.

Overt attention Selectively attending to some part of the surroundings by moving eyes toward this part of interest. Overt attention can be directly observed by employing the eye-tracking technique.

Substance dependence A state caused by administration of addictive substances. This state is characterized by psychological changes (e.g., subjective craving to substances) and physiological changes (e.g., tolerance and withdrawal symptoms). Substance dependence can be diagnosed by structural and semistructural interviews within the frameworks of DSM and ICD systems.

Cognitive neuroscience A promising field that integrates both cognitive science and neuroscience to the understanding of the neural substrates underlying cognitive functions.

KEY FACTS ON ARECOLINE

- The primary alkaloid in raw areca nut.
- Acts on the muscarinic and nicotinic acetylcholine receptors.
- Affects the parasympathetic nervous system, increasing salivation and sweating.
- Has been identified as a chemical carcinogen by the World Health Organization.

SUMMARY POINTS

- This chapter selectively reviews the studies regarding attentional biases in addictive behaviors in general and in betel nut chewers in particular.
- The top-down reward-driven attentional selection has been repeatedly observed in the field of substance use and abuse.
- The visual probe task is a commonly employed task to measure attentional bias toward substance cues.
- The presentation durations of pictures in the visual probe task are manipulated to investigate different phases of attentional processing.
- Ho et al. (2013) showed that heavy chewers exhibited the initial orienting (200ms) and maintained attentional (2000ms) bias toward betel nut cues.
- Betel nut consumption can also affect many aspects of attention and memory acutely and chronically.

REFERENCES


Wang, S. H. (1861). *Cookbook of breath-following house.* Xi’an, China: Sanqun.


