Response Expectancies in a Placebo Study examining Vitamin B

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Cure sometimes; heal often; comfort always

-Hippocrates
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Abstract:

Previous literature has shown response expectancies to be a major determinant of the placebo effect in numerous contexts. There has been no research examining the role of response expectancies in vitamin supplements (such as B₉ & B₁₂), even though multiple meta-analysis have shown supplements to be ineffective in healthy populations. Here we report differing expectations producing differing cognitive results. Subjects (n=54) were divided into three equal groups and presented with stroop, digit span and 15-word memory (delayed & immediate) tasks. Before starting the tasks subjects were presented with a cup of water to drink, yet the symbolic meaning differed between groups. The control group simply ingested water and completed the tasks. The blind group was presented with two cups of yellow sparkling water, they were instructed that one of the cups contained high dose B₁₂, while in reality both cups contained water. The last group was actively deceived. They were presented with one cup of yellow sparkling water and told they were in the high dose Vitamin B₁₂ condition. In both the blind and deceived groups a waiting period, food dye, sparkling water, and the explanation of an expected effect acted to heighten response expectancies. As anticipated, a significant graded effect was found on the stroop task, with the control condition as the slowest and the deceived condition the fastest. None of the memory tasks showed significant differences between the groups, but this might have been due to a small sample size. These results indicate that different verbal instructions about certain and uncertain expectations of Vitamin B’s effects produce different placebo effects, which in turn trigger a change of behavior leading to a significant reduction of time on a stroop task.
Chapter One: Introduction
The Placebo Effect

The placebo effect is a well-documented poorly understood phenomenon; as a result there are a multitude of complex theories that attempt to explain its effect (Pollo et al., 2001, p. 79; Price, Finniss & Benedetti, 2008; de la Fuente-Fernández, Schulzer & Stoessl, 2004; Kirsch, 1985). Not a single social-cognitive, neurobiological, or psychobiological theory can fully explain the placebo and contradictory nocebo effect (Enck, Benedetti & Schedlowski, 2008, p. 195). The history of the placebo effect can be viewed as the early history of medicine since active treatments are rather novel. It is important to understand that ‘the placebo effect’ is a very general term and there are numerous types of placebo responses (Kirsch, 2012). These responses vary greatly in effect size and implore a variety of different mechanisms, depending on the psychosocial context (Price, Finniss & Benedetti, 2008). In a clinical setting placebos are seen as a helpful ally, while in a research setting it is more commonly viewed as a nuisance. While it would be easy to disregard the placebo effect as mere response bias this would be incorrect, as research has shown neurological and physical changes in the brain and body as part of the placebo response (Fields & Price, 2006; Wager, 2005). The placebo effect is unique as it allows the researcher to explore the complexities of brain-mind-body interaction. Research into this phenomenon is still in its infancy, yet recent advances in neuroimaging technology have helped expand physiological understanding, especially in the field of placebo analgesia.
Placebos are usually presented as inert substances, yet this presents a conceptual paradox because an inert substance cannot fundamentally cause an effect. To mitigate this confusion researches studying placebo's influences are essentially examining the effect that the psychosocial context has on a patient’s experience (Price, Finniss & Benedetti, 2008, p. 567). The placebo effect is not static and consistently changes to adapt to the current psychosocial context (Bootzin & Caspi, 2002, p. 126). The two most prominent psychological mechanisms are conditioning and expectancy; these may work together to enhance the effects (Enck, Benedetti & Schedlowski, 2008; Meissner et al., 2011).

As viewed from the psychosocial context, expectancy is a conscious process while conditioning is seen as unconscious (Benedetti, 2009, p. 39). Classical conditioning is due to the pairing of a conditioned stimulus (shape of pill) with an unconditioned stimulus (active drug in pill) to enact an effect (analgesia). In 1985, Kirsch introduced response expectancies, which is “the anticipation of automatic, subjective, and behavioral responses to particular situational cues” (Kirsch, 1997, p. 69). Positive expectations lead to the adoption of responses while negative expectations lead to an inhibition of a response. Response expectancies have been shown to have implications in pain perception, mood states, depression, memory reports, sexual arousal, fear and anxiety, drug use and abuse, asthmatic responses, illness and health along with responses to medical interventions and psychotherapy (Kirsch, 1999, p. 3).
Cognitive Framework of Response Expectancies

Kirsch (1985) incorporated this novel construct into the framework of social learning theory, which was originally developed by Rotter. The social learning perspective holds the view that it is an individual’s interpretation of stimuli, and not the psychical stimuli present, that influences behavior (Bootzin & Caspi, 2002, p. 114). This theory evolved into Bandura’s social-cognitive theory (1989) as more cognitive aspects were added. Bandura differentiated between outcome and efficacy expectations; outcome expectations refer to consequences that follow actions while efficacy is an inherent belief in one’s ability to perform necessary actions to achieve one’s goals. Bandura suggested a focus on broader constructs and stated, “we are now in the era of cafeteria-style theorizing” (Bandura, 1995, p. 354). There is a family of theories referred to as the social-cognitive perspective, which Maddux (1999, p. 33) has stated are not different models but instead variations of a few basic themes. The four basic unifying principles are reciprocal causation, centrality of cognitive constructs, self-regulation and social embeddedness of self and personality. Response expectancies are a complementary addition to this pool of concepts as they distinguish themselves in two distinct ways. Firstly there is the emphasis on nonvolitional responses rather than volitional responses and secondly they’re distinctly self-confirming in nature (Kirsch, 1999, p. 4).

It is important to distinguish between stimulus expectancies and response expectancies. Both types of expectancies are the anticipation of ones reaction to particular behaviors and situations. Yet Kirsch (1997) states the important
characteristic distinguishing response expectancies is that they are directly self-confirming. This is facilitated by the essential ambiguity of internal states, allowing stimuli to be misperceived. The mind builds temporary perceptual sets, which are prone to steadfast expectancy effects (Kirsch, 1999, p. 6). These effects alter a person’s perception to the stimuli, which fundamentally alters the experience. Due to this conceptual framework, the changes of perception, enacted by response expectancies are always accompanied by some physiological changes. Expectations frequently involve multiple differing factors and neurobiological mechanisms. To complete the view of response expectancies a clearer understanding of the social-cognitive perspective is needed.
The neurobiological approach towards the placebo phenomenon attempts to understand how the context of values and beliefs shape and change brain processes which dictate perception and emotion, this in turn effects psychological and physiological health. A central principle is the view that ‘subjective’ placebo constructs have identifiable physiological bases, which modulate internal homeostatic processes. A neuroimaging study, by Wager et al. (2004), showed evidence of prefrontal cortex activity increasing during placebo expectancies, solidifying the notion of expectancies as a functional neurobiological process involving the frontal lobes. It has been proposed that the response expectancy placebo effect is mediated by the brains reward and motivation circuitry. When expectancy creates the possibility for reward, specific cortical neurons then send excitatory glutamatergic inputs to dopaminergic cell bodies (Enck, Benedetti & Schedlowski, 2008, p. 167). Supporting this theory, placebos tend to activate the same cortical areas as reward expectation such as the dorsolateral prefrontal cortex, orbitofrontal cortex, and the cingulate cortex (de la Fuente-Fernandez, Schulzer & Stoessl, 2004, p. 68; Breiter, Aharon, Kahneman, Dale & Schizgal, 2001). De la Fuente-Fernandez et al. (2004) showed tonic activation of prefrontal dopaminergic neurons that project to the dorsal and ventral striatum. Critically, the amount of dopamine released in the dorsal striatum was correlated to perception of clinical placebo effect. The authors concluded that increased dopamine in the ventral striatum is related instead to expectation of reward. In this context the placebo is seen as a reward due to its
positive effects. This was one of the first studies using PET imaging to examine reward circuitry’s involvement in the placebo effect.

Similar research, conducted by Scott et al. (2007), showed a neurological correlation in the nucleus accumbens between placebo responsiveness and responsiveness to monetary reward using PET and fMRI. Mesolimbic dopamine cells activation, in the nucleus accumbens, was also proportionally associated with anticipated and perceived effectiveness of the placebo. These results were interpreted as evidence for the reward circuitry evaluating the ‘incentive value’ and acting as a permission system for the formation of placebo responses (Scott et al., 2007, p. 332). From the nucleus accumbens it is hypothesized that signals are transmitted to other locations involved in the ‘motivation’ network, such as the medial thalamus, amygdala, ventral pallidum and prefrontal cortex (Scott et al., 2007, p. 331). This proposed system would modulate endogenous opioid neurotransmission as seen in placebo analgesia.

Researches have shown that placebo analgesia can reduce pain via opioid and non-opioid mechanisms, yet non-opioid neurotransmission is unknown. Colloca and Benedetti (2005, p. 545) showed the opioid antagonist naloxone could block placebo analgesia yet this was contingent upon the procedure used to induce the placebo effect. The placebo effect could be blocked by naloxone if strong expectation cues facilitated a role, yet when expectation was reduced the placebo effect was resistant to naloxone. Placebo analgesia activates the opioid systems, which affects pain and respiratory centers. Wager et al. in 2004, showed placebo analgesia to decrease pain activity in the medial thalamus, contralateral anterior
insula, and rostral dorsal cingulate. This drastic decrease in the ‘pain matrix’ areas of the brain has been explained as a result of endogenous opioids (Fields & Price, 2006, p. 366). Endogenous opioids have been shown to have extremely precise analgesic effects hinting towards the role of expectancy-mediated precision. Further research by Benedetti and colleagues (2005, p. 10390), adds support to the role of endogenous opioids in expectancy based placebo analgesia effects. The researchers further explain that placebo via conditioning enacts unconscious physiological processes (eg. hormone secretion), while placebo via expectation uses conscious physiological processes (eg. pain or motor performance). This explains the selective results seen by the opioid antagonist naloxone. The current knowledge surrounding the neural circuitry of the placebo phenomenon is far from complete and more research is needed to solidify the role of the reward pathway.
Response expectancy in Placebo Analgesia

The strongest effect size and most heavily experimented aspect of the placebo effect is analgesia (Price, Finniss & Benedetti, 2008, p. 568). Current research clearly shows that experimental manipulation can be used to induce placebo analgesia (Price, Finniss & Benedetti, 2008, p. 570). Montgomery and Kirsch, in 1997, conducted one of the first studies in which expectation of pain levels were manipulated and measured in an experimental setting. Forty-eight undergraduate subjects were conditioned with pain via iontophoretic stimuli. The intensity was reduced in the presence of an inert placebo cream, in an attempt to condition pain relief. After subjects had been thoroughly conditioned they were divided into two groups. The first group, which had no notion of deception, showed an analgesic effect mediated by expected pain levels (49% variance). The second group was informed of the inert properties of the cream, this immediately diminished the placebo analgesic effect (Montgomery & Kirsch, 1997, p. 112). Montgomery and Kirsch's study solidified the notion that conscious expectation is needed for placebo analgesia. One limitation of the study is that it was conducted under a rigorous experimental setting and may not have clinical relevance.

Price and colleagues (1999) used forty undergraduate students to examine differing magnitudes of response expectancy on pre, post, and current pain ratings using heat stimulation. This study helped further the experimental research on response expectancies in placebo analgesia. Methodology consisted of three inert solutions that held differing expectations of pain relief. The first
was presented as a wetting solution and acted as a control. The two other solutions were described as a weak and strong analgesic agent. Expected, concurrent, and retrospective pain in the domains of sensory and affect were measured. The results showed a graded placebo effect in both domains of pain at each time point (Figure I). This graded effect going in the analgesic direction of the powerful placebo (Pain = Control > Weak placebo > Strong placebo) is consistent with the response expectancy theory as it shows the mediating strength of differing expectations. Price and colleagues (1999) furthered the research by confirming Montgomery and Kirsch’s (1997) findings while also demonstrating placebo response expectancy based analgesia in differing types of experimental pain. The authors state the possibility that due to the non-blind nature of experimenters, subtle expectations could have been communicated to the participants. Yet the counterpoint of irrelevance is stressed due to this commonly occurring in a clinical setting. Similarly to Montgomery and Kirsch’s 1997 study, the major limitation is a lack of ecological validity.

**Figure I**

![Figure I](image-url)
In an attempt to bring response expectancy research into a clinical setting, Pollo et al. (2001) derived an experiment showing the strength of response expectancies in thoracotomized patients. This study followed the methodological design used previously by Southwick et al. (1981) to examine expectancies. With this balanced placebo design, half of the participants are told to expect a substance while the other half are told they will receive a placebo. These two groups are then divided again, without their knowledge, and given the active substance or a placebo. The end result is four distinctive groups; active-substance, placebo-substance, active-placebo and placebo-placebo. Due to ethical considerations Pollo and colleagues (2001) adapted this design into three groups; natural history, classic double-blind administration and deceptive administration. Half of the participants in the double-blind condition, the ones that received an active substance, were excluded. The 38 thoracotomized patients, upon request, were treated with buprenorphine to alleviate pain. The experimenters measured subjective pain intensity each hour. All patients were given basal infusions, yet depending on the group experimenters elicited differing expectations. For example, the deceptive administration group had been told by their physician that this placebo was a powerful painkiller while the natural history group had no expectations produced (Pollo et al., 2001, p. 78).

The three groups of patients did not differ significantly for age, weight, sex or type of surgery (Pollo et al., 2001, p. 80). The results showed a significant decrease of buprenorphine dosage between the groups. The deceptive administration group showed a 33.8% decrease of pain medication needed, with respects to the natural history group, while the double-blind group showed a
20.8% decrease. The same graded effect, as seen in experimental analgesic placebo studies, is a consistent finding when looking at the strengths of differing expectations. This research points to methodological flaws in the classic double-blind drug administration paradigm (Pollo et al., 2001; Kirsch & Weixel, 1988; Kirsch et al., 2008). The blind groups intake of buprenorphine, with respect to the control and deceptive group, is almost statistically equal to their perceived chances of receiving the active pain medication (Figure II). The researchers considered the possibility of the patients requesting less dosage due to reassurance caused by the basal infusion. Yet all three groups showed the same pain thresholds upon requesting buprenorphine, essentially showing that requests were triggered by equal amounts of perceived pain. This study provided evidence that differing verbal instructions can cause significant reductions of opioid intake. A critical weakness of the study was a small sample size, yet this was displaced by placebo analgesia’s large effect size.

**Figure II**

![Graph showing total dose of buprenorphine received at the end of the 3-days analgesic treatment in the three groups of patients. The three different verbal instructions about the saline basal infusion produced different buprenorphine intake.](Pollo et al., 2001, p. 80)
The vitamin supplement industry, in the US alone, had yearly sales of 28 billion dollars in 2010 (Guallar, Stranges, Mulrow & Appel, 2013, p. 850). A myriad of Vitamins, including Vitamin B, are sold openly as preventative measures for chronic diseases, cognitive decline and dementia. A recent issue (19th, November, 2013) of the Annals of Internal Medicine published three articles addressing the preventative use of vitamins. The first, Fortmann et al. (2013), conducted a systematic review of the benefits and harms of vitamin and mineral supplements for prevention of cancer and cardiovascular disease. The study found no evidence that supplements affected cancer, cardiovascular disease or overall mortality in healthy non-deficient individuals. This finding contradicted the U.S. preventative services task force recommendation for the use of supplements. Grodstein et al. (2013) conducted a 12-year longitudinal study to determine multivitamins role in cognitive and memory decline in an elderly population. The results of the study showed that daily multivitamin use did not provide cognitive benefits. An editorial accompanying the journal states “we believe that the case is closed— supplementing the diet of well-nourished adults with (most) mineral or vitamin supplements has no clear benefit and might even be harmful.” (Guallar, Stranges, Mulrow & Apple, 2013, p. 851).

The majority of enzymes involved in cellular metabolism consist of a protein (apoenzyme) and an organic coenzyme. These coenzymes are either a B group vitamin or a direct derivative. In a severely malnourished individual deficiency can affect a large range of functions due to a lack of coenzymes. The two enzymes
requiring a B\textsubscript{12} coenzyme are methionine synthase and L-methylmalonyl-coenzyme A mutase (Ball, 2004, p. 387). Vitamin B\textsubscript{12}, which is implemented in cognition, is found in muscle meats, fish, eggs, cheese and milk. Humans are fully dependent on a low dietary intake (1 µg daily) yet the body is extremely efficient at conserving Vitamin B\textsubscript{12} (Green & Miller, 2007, p. 418). Over 80% of Vitamin B\textsubscript{12} is stored in the liver, in the form of adenosylcobalamin. This method of storage is so effective that it takes strict vegetarians at least 20 years to develop signs of deficiency. Therefor, deficiency is rarely caused by lack of Vitamin B and instead a result of absorption failure. Lack of Vitamin B\textsubscript{12} may cause megaloblastic anemia, this is the result of abnormal nuclear maturation caused by impaired DNA synthesis. Vitamin B\textsubscript{9} (folic acid) deficiency causes a morphologically identical anemia (Ball, 2004, p. 374). The functional reasoning behind this condition is a lack of Vitamin B\textsubscript{12} hinders the ability of cells to utilize folic acid for DNA synthesis, ergo causing megaloblastic anemia.

Reynolds (2006, p. 950) states about a quarter of patients with vitamin-B\textsubscript{12}-deficient megaloblastic anaemia have cognitive impairment yet other studies have presented upwards of 50% showing neurological symptoms. Neurological changes are also reported due to the inability to manufacture the lipid component myelin, which then results in demyelination of nerve tissue. The myelin sheath insulates axons, which functionally enables rapid nerve impulses. Neuropathy propagates in peripheral nerves and then progresses to the spinal cord and cerebral hemispheres. Symptoms appear once demyelination reaches deep white matter; these include irritability, memory disturbances, mild depression and apathy. Multiple studies have shown vitamin B\textsubscript{12} deficiency to be
associated with cognitive impairment, while low folate \((B_9)\) concentrations are associated with depression and cognitive decline (Reynolds, 2006, p. 951).

The previous research focused on severely malnourished individuals, yet Vitamin B (specifically, \(B_9\) & \(B_{12}\)) has been touted to improve and increase cognitive function in healthy individuals. These claims are unwarranted; multiple studies have disproven the effectiveness of Vitamin B in deterring disease and improving cognitive function. Huskisson, Maggini and Ruf (2007) published a paper in the Journal of International Medical Research entitled *The Influence of Micronutrients on Cognitive Function and Performance*. The study concluded that micronutrient supplementation might help prevent and maintain cognitive performance. There was no attempt at a systematic review or to grade the evidence. Two of the authors, Maggini and Ruf, work at Bayer, a manufacture of supplements; this is clearly a serious conflict of interest. In contrast, a systematic review published the same year by Jia, McNeill, and Avenell to determine if vitamin, mineral, and fatty acid supplements prevent cognitive decline failed to find significant results. “The meta-analysis showed no significant effect of taking B vitamins or antioxidant vitamins on global cognitive function.” (Jia, McNeill & Avenell, 2007, p. 1).

While the previous studies examined vitamin supplementation in a general sense, a systematic review by Balk et al. (2008) focused on Vitamin \(B_6\), \(B_{12}\) and folic acid \((B_9)\). The researches found fourteen trials that met their criteria, totaling around 50 different cognitive tests for assessment. Some of the most common tests were, in no particular order, stroop, 12 & 15 word immediate and
delayed recall, digit span forward and backward, executive function tasks and speed tasks such as trail making. Stroop is by far one of the most commonly used tests to assess cognitive function, mainly in the domains of selective attention and executive function (MacLeod, 1991, p. 163). Two researchers determined quality by independently grading the trails. If consensus was not reached a third researcher graded the trail to mediate the issue. They then evaluated all outcomes relevant to neurocognitive function. Balk and colleagues (2007, p. 21) concluded that the evidence from Vitamin B supplementation trials does not show any improvement of cognitive function. The authors state a firm conclusion is not possible as the data is sparse.

A study, by Kennedy et al. (2010), attempted to examine the effects of high-dose B vitamin complex with Vitamin C on subjective mood and performance in healthy males. One of the authors, Silvia Maggini, works at Bayer consumer care and the study to examine Berocca®, a Bayer product, was funded fully by Bayer. The participants (n = 220) were divided into a placebo and a vitamin group. They then were presented with psychometric questionnaires, cognitive, and executive tasks. Both groups received identical efferent tablets for 33 days; at the end of the trial measures were repeated. The results showed improved ratings of general mental health, subjective stress and vigor. No significant findings on Stroop and executive tasks were found.

Kennedy and colleagues (2010, p. 66) mention a major limitation of the study is that high-dose Vitamin B leads to discoloration of the urine. This would therefore lead participants to break blind and in turn heighten response expectancies. Only
19 participants reported discoloration of the urine, leading the authors to conclude participants remained blind. While this study showed significant self-report measures in relation to a Vitamin B complex, the lion's share of the research would tend to disagree with this finding. It is also important to stress that the study found no significant results on measures of cognitive or executive control.
Response Expectancy in Vitamin Supplement Contexts

There is a serious lack of experimental research on placebo response expectancies role in vitamin supplementation. More specifically there is not a single study using Vitamin B to examine placebo response expectancies. The closest relatable study is the investigation of another cognitive enhancer, caffeine. Kirsch and Weixel in 1988 examined perceived influence of caffeine on cognitive, physiological, and subjective measures. Subjects were randomly allocated in a double-blind administration group or a deceptive administration group and given varying doses of decaffeinated coffee. Similarly to Pollo et al. (2001), it was hypothesized that deceptive administration would elicit greater expectations than the double-blind administration group, ergo creating a greater placebo effect. The researches also predicted a curvilinear ‘dose’ effect, as large apparent doses may be limited by credibility and the validity of small doses would be questioned. One hundred undergraduate psychology students that were self reported coffee drinkers (3.2 cups per day) participated in the study. The first experimenter was blind to group assignment and collected data on self report, behavioral, and physiological measurements pre and post consumption. The second experimenter administered the decaffeinated coffee and instructed the participants to wait 20 minutes. This wait time helped increase the subjects perceived validity of having consumed caffeinated coffee.

Subjective mood was measured by means of a likert scale; pre and post consumption. Physiological and behavioral variables were assessed pre and post placebo consumption. The behavioral measures used were digit span (forward),
reaction time, symbol substitution and rotor pursuit. Kirsch and Weixel (1988, p. 320) asked subjects, during pre placebo assessment, to predict the effects of coffee on behavioral measures. After post placebo assessment subjects were asked to estimate the likelihood that the coffee was caffeinated. These measures were critical controls to establish response expectancies role in reported changes of behavior. Analysis revealed significant placebo responses on the variables alertness, tension, pulse-rate and systolic blood pressure. There was a failure to find significant between-group effects on behavioral measures. Kirsch and Weixel (1988, p. 322) explain this was due to subjects being divided on the reported effects of caffeine consumption. Interestingly, post hoc analysis showed that beliefs about the effect of caffeine had strong correlation to actual results.

Further research in the area of caffeine related response expectancies by Colagiuri and Boakes (2009) built upon the previous theories while also adding the nootropic Piracetam. The researchers conducted two experiments (caffeine & piracetam) with the goal of examining positive feedback’s influence on cognitive performance. Another major aim of the study was to examine the efficacy of the commonly used random control trail (RCT). This was the first study “to show that observable improvement does influence perceived treatment” (Colagiuri et al., 2010, p. 439). Subject’s belief of receiving an active substance was positively correlated with cognitive performance. Both of the articles, Kirsch et al. (1988) & Colagiuri et al. (2010), provide solid evidence of the role of placebo response expectancies in daily use enhancing drugs. The implications that both of these studies present, along with numerous other
response expectancy research relating to the efficacy of RCT, will be expanded upon in the discussion.
Current Research Aims

This literature review took a three-pronged approach. Firstly by focusing on placebo response expectancies in the most studied domain, analgesia, to develop a fundamental understanding of the variables needed to elicit response expectancies. Secondly the review examined supplement research, specifically Vitamin B, to show a disputed amount of cognitive enhancement research, leaning heavily on non-significant results. Finally resulting in the examination of previous response expectancy research in the field of cognitive enhancing substances.

Due to this critical lack of response expectancy research in the domain of vitamin supplementation, I propose an experiment to fill this void using the ethical placebo design (Pollo et al., 2001; Kirsch & Weixel, 1988). As previous research has shown the effectiveness of cognitive enhancement is questionable at best, the contradicting reports may be due to varying response expectancies. The methodological issue of discolored urine could possibly be enhancing the response expectancy effect leading to superfluous results. This study will use three of the most common cognitive measures for vitamin supplement studies; Stroop, 15-word immediate and delayed memory recall and digit span. Three Likert scales will be implemented to specifically examine the domain of response expectancy strength. The fundamental aim is to determine the presence and strength of placebo response expectancies in a Vitamin B enhancing psychosocial context.
Hypotheses:

On Placebo Vitamin Effects

Hx_1 - A significant difference will be found between the experimental administration group, blind administration group and the control group on the stroop task.

Hx_2 - A significant difference will be found between the experimental administration group, blind administration group and the control group on the memory tasks; immediate 15-word memory recall, delayed 15-word memory recall and digit span.

On strength of Response Expectancies

Hx_3 - Vitamin B’s perceived effectiveness and belief of consumption measured by a likert scale will be higher in the deceptive administration group then the blind group.
Chapter Two: Methodology
Participants

Multidisciplinary college students of all ages (m = 22.7) were used to conduct this study. To achieve a power of 0.8, 52 participants were required. A medium effect size was chosen due to the substantial variability in placebo effect sizes, “-0.95 to +0.57” (Price, Finniss & Benedetti, 2008, p. 568). A total of fifty-four students participated and were divided into three groups, therefore each group contained 18 subjects. The sample consisted of 28 male (52%) and 26 female (48%). The control groups mean age was 22.9 (range = 25, SD = 5.8), the blind groups mean age was 24.2 (range = 27, SD = 6.3), and experimental groups mean age was 21.2 (range = 5, SD = 1.2). The groups did not significantly differ in age ($\chi^2(2) = 4.43, p = .11$). The participants were selected through convenience and verbal recruitment. While any currently attending Irish college student was welcome, a large number of psychology students participated. No incentives were used and every subject participated out of their own volition.
A true experimental design was utilized as participants were divided into three groups. This division into groups was based on order of recruitment, therefore it acted as random allocation. The independent variable was group assignment; either control group, blind administration group or deceptive administration group. Therefore utilizing Pollo and colleagues (2001) ethical adaptation of a balanced placebo design. The dependent variables are the presented tasks; immediate memory recall, digit span, stroop task and delayed memory recall. Additional dependent variables were used to determine the efficacy of the experiment by measuring for perceived pretest Vitamin B effectiveness, perceived posttest influence and perceived posttest consumption.
Materials & Apparatus

Plastic cups filled with sparkling water and three drops of yellow food coloring optimally imitated Vitamin B. A pilot G2 black gel pen was provided for participants. Other materials included a test tube and dropper for the yellow food dye.

Response Booklet:

The booklet contained (in order of presentation) a title sheet, study information sheet, consent, demographics, a 6-point pre-test belief of Vitamin B effectiveness likert scale, two 15 word memory recall lists on separate pages (immediate & delayed), two 7-point post-test likert scales for perceived influence and consumption of Vitamin B along with a debrief form. The demographic sheet for the participants included categories for sex, age, allergies, race and current level of college. On the same page, as seen in the appendix (p. 64), a 6-point likert scale asking pre-test belief of effectiveness on Vitamin B’s role in cognitive enhancement was presented. This scale consisted of the responses: definitely enhancing, moderately enhancing, no difference, moderately impairing, definitely impairing and not sure/no opinion.

The next two pages each consisted of 15 blank lines used for both memory recall tasks. Following these pages were two seven-point post exam likert scales. The first intended to determine perceived effectiveness by asking the question “Do you think the Vitamin B you were given helped your performance on the
memory and attention tasks?” (See appendix p. 67). The responses of performance ranged from a definite increase to a definite decrease. The second intended to determine if deception was successful by asking, “Do you think you consumed Vitamin B?” (See appendix p. 67). The responses on belief ranged from certainly Vitamin B to certainly not vitamin B.

Tasks:

Two of the tasks, digit span and stroop, used the Psychology Experimental Building Language (PEBL) software therefore data was automatically digitized. An early 2011 MacBook pro running Windows 8, through parallels, was used to run the PEBL software. The program divided the stroop task into three parts; each sub-section contained 24 stimuli. The first two sections were used to get the participant comfortable to the program; no data was analyzed. The first section contained 24 stimuli points presented as round colored dots while the second section contained 24 random words in color. To make the stroop task easier, adhesive colored bookmarks were placed on the corresponding keys. The final section had 24 color words in incongruent colors, as seen in figure III. The program would not let the participant move to the next word without the correct answer; ergo adding significant time to the result. The digit span task individually presented numbers while in tandem verbally reciting them. At the end of the digit string, participants were expected to type in order the previously presented digits using the keyboard, this would result in a ‘correct’ or ‘incorrect’ response from the program. The program started with a 3 digit long span and
after two correct responses would extend the span by a digit. This continued until the responder made two mistakes on the same digit string.

**Figure III:** PEBL launcher stroop part three

Microsoft PowerPoint 2007 was used to present the Rey memory list. The first slide was blank; this functioned as a control for the participants viewing the slides before the presentation began. After this slide, fifteen words were presented for three seconds each. The words sourced from Rezvanfard and colleagues (2011) included the following, in presentation order: Desk, Ranger, Bird, Shoe, Stove, Mountain, Glasses, Towel, Cloud, Boat, Gum, Pencil, Church, Fish and Lamb. The final slide contained the phrase ‘Please write the words you remember’. The response booklet was used to record all the words the participants remembered.
Procedure

Every participant was tested in a study room in the Dublin Business School (DBS) library. The length of sessions varied slightly depending on the participant's general speed. Subjects were initially casually asked how much they knew about the experiment. This acted as a controlling factor to determine if deception would be possible. Another controlling variable, mainly to heighten priming, was the exclusion of subjects that consumed supplements 24hrs prior to the experiment. After these two conditions were satisfied, the group to which they had been assigned to, via recruitment, was explained to them. Following this explanation, priming varied between the groups yet the procedure and explanation of the tasks was consistent.

Control Group Priming Procedure

After explaining to the subject that they were assigned to the control group, therefore no consumption of Vitamin B would be necessary, the response booklet was presented. While the subjects read over the information sheet (see appendix p. 62), which explained effects of Vitamin B, it was again verbally stressed that they are in the control group.
Blind Group Priming Procedure

After explaining to the subject that they were assigned to the blind group, therefor there would be a 50% chance of consumption, the response booklet was presented. While the subjects read over the information sheet (see appendix p. 62), which explained effects of Vitamin B, the experimenter also verbally explained expected effects. Due to the tasteless nature of the placebo it was explained that both cups look and taste the same and differentiation is impossible. After consent was obtained the student was asked to choose a cup. Following consumption a waiting period of around four minutes helped heighten response expectancies. During this time any questions were clarified and the tasks were briefly explained. The procedure of the tasks was the same between all groups and is clarified in more detail bellow.

Experimental Group Priming Procedure

After explaining to the subject that they were assigned to the experimental group, therefor consumption of Vitamin B would be necessary, the response booklet was presented. While the subjects read over the information sheet (see appendix p. 62), which explained effects of Vitamin B, the experimenter also verbally explained expected effects. Due to the tasteless nature of the placebo it was explained that the high does Vitamin B supplement has no taste. After consent was obtained the student was asked to consume the yellow sparkling water. Following consumption a
Waiting period of around four minutes helped heighten response expectancies. During this time any questions were clarified and the tasks were briefly explained. The procedure following group orientation was the same between all groups and is clarified in more detail below.

Subjects of all groups were uniformly explained the tasks, once briefly while waiting for the substance to take effect and then in more depth before each of the tasks. The order was explained, so subjects would understand and expect delayed memory recall at the end. The experimenter also explained that fifteen words would be individually presented on the screen and at the end to write down, in any order, all the words remembered. The next task was the stroop task, which was the most complicated to describe therefore did not commence until subjects possessed a complete understanding of the task. It was explained multiple times that speed is important yet to not disregard accuracy as it will add time due to the task not continuing. In addition to a verbal description of the complete task, the PEBL software explained each subsection of the test on the screen.

The third task measured digit span using PEBL. Like the procedure of the stroop task participants had verbal instructions in addition to the PEBL on screen instructions. The experimenter mentioned to each participant that multiple digit span mistakes are allowed. Upon completion of the digit span, participants were instructed to rescribe the words they remembered from the earlier presentation;
this task was limited to two minutes. Following completion of all the tasks participants moved on to complete both posttest likert scales.

Due to the anonymous nature of the study consent was granted via continuation. Deception was used in two of the three groups, therefore debriefing was necessary. The last page of the response booklet contained a debriefing prompt, as seen in the appendix on page 67. The subjects were also verbally explained about the use of deception and asked if they wish to withdraw their data, no participant availed this option.
Chapter 3: Results
Statistically Analysis

The first step of the statistical analysis determined whether the scale variables contained parametric qualities. This was achieved by running normality tests and plots in Statistical Package for the Social Sciences (SPSS). A Shapiro-Wilk normality test revealed three of the four scale variables to be non-normal; Stroop, Digit Span and Immediate memory. Boxplots revealed two extreme outliers in the stroop variable, one in the blind group and the other in the experimental group. After controlling for these outliers, the two groups became normally distributed. For immediate memory, the control group possessed non-normal qualities while the blind group possessed non-normal qualities for digit span scores. Descriptive statistics were then run for each dependent variable, mainly to determine directionality.

For the first hypothesis, relating to stroop times, a one-way ANOVA was appropriate. This test was chosen due to the parametric qualities of the data along with the need to determining differences between multiple groups.

For the second hypothesis, examining memory, multiple tests were needed for each dependent variable. The first memory task, immediate memory, a Kruskal Wallis analysis was used due to the non-normal qualities of the control group. The same test was run for digit span scores, as they also possessed non-normal qualities. For delayed memory a one-way ANOVA was appropriate due to the normal distribution of data in conjunction with need to examine multiple groups.
For the final hypothesis, examining perceived influence and consumption, two Mann-Whitney U tests were necessary due to the ordinal qualities of the data.
### General Sample & Group related statistics

**Table 1: Within Sample Descriptive Statistics**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>N</th>
<th>Mean Age</th>
<th>Pretest Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>28</td>
<td>26</td>
<td>54</td>
<td>22.8</td>
<td>4</td>
</tr>
</tbody>
</table>

Although participant demographics have already been presented (see page 29), they may be viewed above (table 1). A Kruskal-Wallis analysis determined no significant between group differences of age ($\chi^2(2) = 4.43, p = .11$). The majority of the sample ($n = 34$) marked ‘Moderately enhancing’ (Mode = 4) on pre-test Vitamin B effectiveness.

The two extreme outliers on Stroop scores can be viewed on the stem and leaf plot below (Figure IV). The first outlier number 26 belongs to the blind group while the second outlier, number 12, belongs to the experimental group. After excluding these two extreme outliers the two respective groups showed normality on the Shapiro-Wilk test.

**Figure IV: Stem & Leaf Plot of Stroop Times showing outliers**

![Stem & Leaf Plot of Stroop Times showing outliers](image-url)
Hypothesis one (Hx₁): Stroop- Descriptive and Inferential Statistics

Table 2: ANOVA table on Stroop times

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>F</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>29.76</td>
<td>9.05</td>
<td>18</td>
<td>4.46</td>
<td>(2, 49)</td>
<td>.017</td>
</tr>
<tr>
<td>Blind</td>
<td>24.61</td>
<td>7.02</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>22.61</td>
<td>5.31</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As anticipated, a graded effect in order of condition via strength of response expectancy was observed. As seen in Table 2, the control group took the longest time to complete the task, followed by the blind group, while the experimental group out preformed the other groups. This downward trend between groups trend is best represented in Figures V, which illustrates mean differences in seconds on stroop times. Another graph illustrating these trends, in the form of a violin plot, can be seen in the discussion (p. 50); the statistical package R was used. A violin plot is the combination of a box plot and a kernel density plot, therefore was used to best illustrate the between group difference on stroop times. To see the command line used to build the graph see page 61 of the appendix.
One-way ANOVA ($F (2, 49) = 4.46, p = .017$) showed significant differences between groups on stroop times (see table 2). Due to the minimum amount of means needed to for a one-way ANOVA, three, the more liberal Fisher's LSD test was chosen. Post hoc analysis confirmed that the difference were significant in nature between the control group ($M = 29.76, SD = 9.05$) with the blind group ($M = 24.61, SD = 7.02, p = .043$) and with the experimental group ($M = 22.61, SD = 5.31, p = .006$). No significance differences were found between the blind and the experimental group.
**Hypothesis two (Hx₂): Memory**

**Immediate Memory - Descriptive and Inferential Statistics**

**Table 3**: Kruskal-Wallis Table on Immediate Memory

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>(\chi^2)</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8.56</td>
<td>2.12</td>
<td>18</td>
<td>3.12</td>
<td>2</td>
<td>.21</td>
</tr>
<tr>
<td>Blind</td>
<td>9.67</td>
<td>2.09</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>9.17</td>
<td>2.31</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As seen in Table 3, there was no graded effect between the control (M = 8.56, SD = 2.12), blind (M = 9.67, SD = 2.09) and experimental group (M = 9.17, SD = 2.31). A Kruskal-Wallis one-way ANOVA test showed that the groups did not differ significantly on immediate memory scores \(\chi^2(2) = 3.12, p = .21\).

**Digit Span - Descriptive and Inferential Statistics**

**Table 4**: Kruskal-Wallis Table on Digit Span

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>(\chi^2)</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.89</td>
<td>1.41</td>
<td>18</td>
<td>1.64</td>
<td>2</td>
<td>.44</td>
</tr>
<tr>
<td>Blind</td>
<td>6.72</td>
<td>1.07</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>7.17</td>
<td>0.99</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As seen in Table 4, there was no graded effect between the control (M = 6.89, SD = 1.41), blind (M = 6.72, SD = 1.07) and experimental group (M = 7.17, SD = .99). A Kruskal-Wallis one-way ANOVA analysis showed that the groups did not differ significantly on digit span scores \(\chi^2(2) = 1.64, p = .44\).
**Delayed Memory – Descriptive and Inferential Statistics**

**Table 5: ANOVA Table on Delayed Memory**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>F</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.72</td>
<td>2.89</td>
<td>18</td>
<td>2.1</td>
<td>(2, 51)</td>
<td>.13</td>
</tr>
<tr>
<td>Blind</td>
<td>8.39</td>
<td>2.45</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>8.06</td>
<td>2.36</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As seen in Table 5, there was no graded effect between the control (M = 6.72, SD = 2.89), blind (M = 8.39, SD = 2.45) and experimental group (M = 8.06, SD = 2.36). A one-way ANOVA test showed that the groups did not differ significantly on delayed memory (F (2, 51) = 2.1, p = .13).

The graph below (Figure VI) clearly illustrates the lack of graded effects of groups across all memory variables.

**Figure VI: Mean scores of groups on each memory variable**
**Hypothesis three (Hx3): Strength of Response Expectancy**

*Posttest Perceived Effectiveness*

A Mann-Whitney U analysis was used to test the hypothesis that there would be a significant difference of posttest perceived effectiveness of Vitamin B between the blind and experimental group. The blind group had a mean rank of 17, compared to the mean rank of 20 for the experimental group. The Mann-Whitney revealed that the blind and experimental group did not differ significantly (U = 135, p = .352).

*Posttest Belief of Consumption*

A Mann-Whitney U test was used to check the hypothesis that there would be a significant difference of perceived consumption of Vitamin B between the blind and experimental group. The blind group had a mean rank of 14.14, compared to the mean rank of 22.86 for the experimental group. The Mann-Whitney revealed that the blind and experimental group did differ significantly (U = 83.5, p = .011).
Chapter 4: Discussion
The purpose of this discussion is to clarify and concisely examine the results. To accomplish this task most effectively, performance on tasks in the domains of cognition (Hx₁) and memory (Hx₂) will be grouped together. The second part will examine the strengths of the response expectancy (Hx₃), which effected the tasks. Results and findings of these sections will be compared and contrasted to the previous findings, mainly response expectancy based, which have been already discussed at length in the literature review. The author will then discuss the implications of the data, followed by and examination of strengths and weaknesses. The discussion will then conclude by presenting future directions for response expectancy research in general along with the more specific domain of Vitamin B’s role in this field.
Cognition and Memory Tasks (Hx₁ & Hx₂)

The aim, to determine the presence and strength of placebo response expectancies in Vitamin B, was partially supported by significant results in Stroop times. Due to the lack of research on Vitamin B placebo response expectancies the results provided should be interpreted conservatively. Two of the three memory tasks were non-normally distributed, which may be indicative of an insufficient sample size. The across board lack of memory task significance could be explained in two ways. Firstly, that word and digit memory cannot be significantly altered via placebo response expectancies. This validation of the null hypothesis is supported by Kirsch and Weixel’s (1988) non-significant findings pertaining to caffeine response expectancies on digit memory. The second explanation of these results, also stated by Kirsch and Weixel (1988), could be the limited magnitude of effect in the domain of memory. Further research is needed on the influence of response expectancies on memory, along with more specific research examining this phenomenon in a Vitamin B context.

The overwhelming majority of students, 63%, stating Vitamin B supplements are moderately enhancing, in clear contradiction with current research findings, is a validation of the experiment in its self. The between group graded effect on stroop times, as seen in the violin plot bellow (Figure VII), is in agreement with the theoretical underpinnings of placebo response expectancies. Results clearly indicate that the differing placebo Vitamin B responses on the Stroop task were due to differing verbal instructions. These verbal instructions altered the psychosocial context, specifically pertaining to the symbolic meaning for what
was in actuality a cup of yellow sparkling water. The differing strengths of these intentionally contrived false assumptions, which participants held, led to an equivocal strength placebo effect. Previous placebo research in other fields, such as analgesia and caffeine, Pollo et al. (2001) and Kirsch & Weixel (1988) respectively, have demonstrated this graded placebo response.

**Figure VII: Violin Plot of Stroop Scores**

![Violin Plot of Stroop Scores](image)

Post hoc tests revealed significant differences between the control to the blind and experimental groups. Therefore, no significant difference was found between the blind and experimental group, this is in agreement with the non-significant finding ($H_{x3}$) of differing expectancies between the groups. Due to the trending nature of results, along with previous research, it is probable that the sample size is to blame for these non-significant results. It is theorized by the
author that selective attention, as measured by the stroop task, may be a more malleable cognitive construct than memory, ergo more susceptible to response expectancy mediated placebo effects.

**Strength & Weakness of reported Response Expectancies (Hx₃)**

The third hypothesis pertaining to conscious effect and consumption belief of Vitamin B was partially supported. The primary function of these measures was to determine the role and strength of response expectancies in the current study. As already stated, there was no difference in perceived effectiveness between the blind and experimental groups. As response expectancies are inherently non-volitional this result is not surprising. It is also in agreement with the early results, which show no task difference between blind and experimental groups. There was a significant difference of belief of consumption between the blind and experimental groups, showing that deception was effective. A few participants in the experimental condition foresaw deception, as the population was well educated this was expected, yet clearly not statistically significant.

**Limitations**

The study suffered from an over reliance on psychology students, therefore it might not be an accurate representation of the student population. As with any lab orientated experiment ecological validity is an issue. A non-blind
experimenter was incorporated within the study and used as a psychosocial variable to enhance response expectancies. While this methodology is unorthodox it has been argued as a logical addition to response expectancy research (Price et al., 1999, p. 155). In future response expectancy based Vitamin B studies, a flavor additive is recommended to further strengthen the placebo effect.

**Implications**

The results of this study help explain the massive expenditure on Vitamin supplements. While inherently Vitamin B may hold benign and passive properties, the expectations attached have very noticeable results, thus propagating continual use. This assists in explaining the prevalence, use and contradictory findings surrounding Vitamin B as a cognitive enhancer in healthy individuals. The field of medicine can exploit these placebo factors to enhance the effectiveness of active treatments. Pollo et al. (2001) clearly showed the clinical utilization of response expectancies to reduce opioid intake. Due to many active treatments possessing negative side effects, a slight substitution of less active medication with enhanced expectancies would benefit patients. The placebo effect is an ethical minefield, as true informed consent negates possible beneficial outcomes.
The more serious implication that the findings show, along with support from response expectancy findings in other fields, the ineffectiveness of the current gold standard of drug assessment, the random control trial (RCT). The majority of Vitamin B studies use the classic double blind experimental procedure, which Kirsch and Weixel (1988) state their “data challenge(s) the validity of double-blind experimental designs and suggest that this common method of drug assessment may lead to spurious conclusions” (p.319). This can be best illustrated using Kennedy et al. (2010) findings of cognitive improvements using high-dose Vitamin B. This excessive use of Vitamin B noticeably discolors the urine of active-group participants. If these participants break blind, usually as a result of a physiological change, this in turn increases response expectancies. There in lies a paradox as the more effective a treatments is, the more noticeable are the effects, or lack there of, which increases the difficulty in assessing validity using a RCT (Colagirui & Boakes, 2009, p. 433). Active placebos, which mimic the corresponding treatments’ side effects, can be employed to counter this breaking blind phenomenon.

As discussed earlier, a balanced placebo design is one of the most effective drug assessment techniques. This design allows the examination of the pure effect size of the substance, pure effect size of corresponding response expectancies, the combination of both and a control. There are ethical issues surrounding the use of this design, as it implores the active deception of participants. The medical community must come to a consensus towards the ethical use of placebos.
Further Research

As this study is one of the first to examine placebo response expectancy in a Vitamin B context, research is needed with a larger sample size to solidify the expectancy mediated Stroop performance results. The domain of memory in relation to response expectancies is largely unknown; more research is needed to determine if response expectancies can alter memory. One of the most important directions future response expectancy research should examine is clinical implementation. This utilization of placebo response expectancies, as demonstrated in analgesia, should expand to other illnesses.

Conclusion

The present study sheds some light on the continual use of vitamin supplements in a healthy population. While it is challenging to draw assumptions on the non-significance of memory, mainly due to a lack of response expectancy based research, the Stroop task offers insight into expectancy-based alterations of cognition. These findings carry grave implications on the efficacy of the double-blind procedure, especially when pertaining to active drug evaluation. In conclusion, the author stresses the utilization instead of the prohibition of response expectancies in the clinic.
References:


Appendix:

R Statistics – Violin Plot Command

\[
\text{with(ds,vioplot(stroop[group==1], stroop[group==2], stroop[group==3],} \\
+ \text{ names=c("Control Group", "Blind Group", "Experimental Group"),col=0))} \\
> \text{with(ds,vioplot(stroop[group==1], at=1, col = "tomato1",add=TRUE))} \\
> \text{with(ds,vioplot(stroop[group==2], at=2, col = "skyblue",add=TRUE))} \\
> \text{with(ds,vioplot(stroop[group==3], at=3, col = "goldenrod1",add=TRUE))} \\
> \text{title(xlab="",ylab="Time in Seconds",main="Violin Plot of Stroop Scores")}
\]
Vitamin B Cognitive Enhancement Study

Intake Form
Vitamin B as a Cognitive Enhancer
Informed Consent

You are invited to participate in a research study that will form the basis for an undergraduate thesis. Please read the following information before deciding whether or not to participate.

What are the objectives of the study?
The nature of this study requires participants to be slightly naive to the exact research question, as information about the research may influence your behaviour and responses. For this reason we can only inform you that we are conducting research on the cognitive enhancing effects of Vitamin B.

What are the effects of Vitamin B?
There are no physiological effects from the ingestion of Vitamin B, yet cognitive enhancing effects are expected. These slightly enhancing effects will dissipate with time. There are no known negative effects from Vitamin B, as it is regularly found in food.

What does participation involve?
Participation involves the ingestion of Vitamin B, along with the administration of cognitive tasks. You will be fully debriefed at the end of the experiment.

Right to withdraw
Participants have the right to withdraw from the research at any time for whatever reason. Participants can also request at any time to have their response data removed from record.

Are there any benefits from my participation?
While there will be no direct benefit from participation studies like this can make an important contribution to our understanding the enhancing effects of Vitamin B. As such, the findings from this study may be presented at national and international conferences and will be submitted for publication in peer-reviewed journals. Interim and final reports will be prepared. However no individual participant will be identified in any publication or presentation and the data used will be anonymous. Individuals will not be offered any monetary or other rewards for their participation.

Are there any risks involved in participation?
There are no risks associated with participation. Any inconvenience involved in taking part will be limited.

Confidentiality
All individual information collected as part of the study will be used solely for experimental purposes. They will be stored safely and will not be publicly displayed or published without prior consent.

Contact Details
If you have any further questions about the research you can contact:

Researcher:  Supervisor:
Nicholas Judd            Rosie Reid
Consent Form
Vitamin B Cognitive Enhancement study.

I have read and understood the attached Information Leaflet regarding this study. I have had the opportunity to ask questions and discuss the study with the researcher and I have received satisfactory answers to all my questions.

I understand that I am free to withdraw from the study at any time without giving a reason and without this affecting my training.

By proceeding I agree to take part in the study.

- Please take the substance before continuing, so there is time for it to take effect.
Demographic Information

Subject Number:

Age –

Sex –

Race –

Level of education –

Allergies –

Circle how effective do you think Vitamin B is as a cognitive enhancer?

○ Definitely Enhancing

○ Moderately Enhancing

○ No difference

○ Moderately Impairing

○ Definitely Impairing

○ Not sure/No opinion

-Wait 3 minutes for the substance to take effect, if you have any questions ask them now!
Word Recall Sheet

1) ______________________________
2) ______________________________
3) ______________________________
4) ______________________________
5) ______________________________
6) ______________________________
7) ______________________________
8) ______________________________
9) ______________________________
10) ____________________________
11) ______________________________
12) ______________________________
13) ______________________________
14) ______________________________
15) ______________________________

- Administer Digit Span
- Administer Stroop Task
Delayed Word Recall Sheet

1) ______________________________
2) ______________________________
3) ______________________________
4) ______________________________
5) ______________________________
6) ______________________________
7) ______________________________
8) ______________________________
9) ______________________________
10) _____________________________
11) _____________________________
12) _____________________________
13) _____________________________
14) _____________________________
15) _____________________________
Post Test Questionnaire

Effectiveness:

Do you think the Vitamin B you were given helped your performance on the memory and attention tasks?

- Definite increase in performance
- Probable increase in performance
- Possible increase in performance
- No increase in performance
- Possible decrease in performance
- Probable decrease in performance
- Definite decrease in performance

Consumption:

Do you think you consumed Vitamin B?

- Certainly Vitamin B
- Probably Vitamin B
- Possibly Vitamin B
- Not sure
- Possibly not Vitamin B
- Probably not Vitamin B
- Certainly not Vitamin B
Debrief/Study Information Sheet

This study used deception to study the response expectancy of the placebo effect; deception was absolutely critical to obtain an accurate measure. The study was measuring if the expectancy of the effect of Vitamin B produced noticeable cognitive effects. If this makes you uncomfortable as per your wishes your data may be withdrawn from the study.

Nicholas Judd

Also verbally present the debrief prompt.

There was no Vitamin B, it was harmless sparkling water with yellow food colouring! If you have any questions do not hesitate to ask, this research potentially has profound impact and your participation was greatly appreciated. Thanks!