Scientific Research

Aromas of *Salvia* Species Enhance Everyday Prospective Memory Performance in Healthy Young Adults

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Abstract

Research has previously demonstrated that aromas of both *Salvia officinalis* and *Salvia lavandulaefolia* are capable of modulating aspects of retrospective memory, attention and mood. This study is the first to report the potential for these aromas to enhance everyday prospective memory performance in healthy young adults. In an independent groups design, three conditions, *Salvia officinalis* aroma, Saliva *lavandulaefolia* aroma and no aroma were employed with 45 healthy volunteers in each condition. Prospective memory performance was assessed using the Prospective Remembering Video Procedure. Data analysis revealed that the *Salvia officinalis* aroma group performed significantly better than the control group on both event and action subscales of the prospective memory task. *Saliva lavandulaefolia* aroma only led to enhancement for the event measure when compared to controls. No differences were found between the aroma conditions. These findings offer support for those previously reported for the effects of the aromas of *Salvia* sp. on cognition and again demonstrate differential effects of the two aromas. The results are considered in terms of pharmacological mechanisms.

1. Introduction

History records the extensive use of herbal medicines and other plant derived products for the treatment of

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health problems, and the improvement of day to day living. However, the development of synthetic drugs, often from analogues of natural compounds, overshadowed the use of herbal therapeutics [1]. Recent times have witnessed a resurgence of such alternative therapies, with alternative herbal medicines being used along side or instead of the more conventional treatments [2], with one of the main focuses being the attempt to find treatments to combat age-associated cognitive decline [3].

Of interest in this respect has been the *Salvia* genus, in particular *Salvia officinalis* (SO) and *Salvia lavandulaefolia* (SL). Although relatively new with respect to systematic scientific research the findings reported to date regarding the efficacy of extracts of these species have been very promising. The demonstrations that extracts of *Salvia* sp. possess acetylcholinesterase inhibitor properties [4]-[6] suggest a potential for cognitive modulation, and some investigations of clinical effects have been made in relation to such properties. For example [7], administered an alcoholic extract of SO leaf in a double blind intervention for mild to moderate Alzheimer's disease over a four month period. The authors reported significantly improved cognitive ability and decreased agitation when compared to the placebo control group.

A body of research has also been directed at performance and mood effects in healthy young volunteers. Kennedy *et al.* [8], administered an extract of SO prior to completion of defined intensity stressor battery and reported significantly improved performance on the Stroop sub-task, and positively modulated mood in the higher dose SO group. Similarly, Tildesley [9] administered SO extracts to healthy young volunteers and reported significantly enhanced word recall for various doses of SO when compared to the placebo control group. Additionally, a study employing older participants found significant improvements following SO administration for the quality of memory and the quality of attention factors derived from the Cognitive Drug Research (CDR) cognitive assessment system [10]. This study however did not find any effects for self-reported changes in mood indicating that the potential for cognitive enhancement is not necessarily dependent on changes in subjective state.

Studies of *Salvia lavandulaefolia* have also provided converging evidence regarding the efficacy of the *Salvia* genus. Tildesley, *et al.* [11] orally administered SL essential oil and the findings suggested dose dependant memory enhancements, with the major improvements in word recall being for 50 µl dosage group. In a second study, participants were given either a placebo or 25 µ or 50 µ of SL essential oil. The CDR system was again used to assess cognitive function at 1, 2.5, 4 and 6 hours following administration. Significant improvements were found for both doses of the SO essential oil when compared to the placebo group. Specifically improvements were reported for the secondary memory and speed of memory factors—although at differing time points and doses [12].

There is currently a new momentum in the research of essential oils, with an increasing focus on the aromas of the essential oils and their putative effects on cognitive ability and mood. Employing the CDR assessment system, Moss *et al.* [13], reported that the aromas of Lavender and Rosemary essential oils produced differential effects for the quality of memory factor, and significant enhancements were seen for Rosemary on the secondary memory factor compared to both Lavender and no aroma control groups. Mood assessments were also significantly affected, with rosemary producing increased alertness and contentedness. Further to this, Moss and colleagues found that peppermint aroma resulted in significantly improved quality of memory when compared to ylang-ylang aroma and a no aroma control group [14]. These findings were found not to be associated with changes in mood measurements. It has been suggested that the aromas of essential oils may have similar effects as oral ingestion of plant extracts as a consequence of the absorption of volatile active components via the lungs. This follows the work of Kovar *et al.* [15] who found significant increases when monitoring locomotor activity in rats after oral administration of rosemary; A finding that was mirrored after the inhalation of rosemary aroma. This evidence might suggest that when the aromas of *Salvia* sp. are inhaled, enhancements in cognitive abilities of a similar magnitude and manner to those observed when herbal extracts are taken orally could be seen. Indeed, Moss *et al.*, report a study that investigated the effects of *Salvia* sp. aromas, and make a qualitative comparison to those previously reported for oral administration of the herbs concluding that a general, but not universal, picture of similar effects was present [16]. Furthermore, in a recent study significant correlations were found between plasma borne 1,8-cineole and cognitive performance following exposure to rosemary aroma [17], strongly supporting the contention that aromas may act pharmacologically.

Prospective memory (PM) is an important aspect of everyday functioning, being the ability to remember to do something at some point in the future [18]. A failure of prospective memory can have a range of consequences, such as forgetting an appointment or to take prescribed drugs at appropriate times. An increasing amount of re-

search has been focussed on the decline in PM in old age and dementia with evidence of decline, exaggerated in dementia patients, coming from both questionnaire [19] and naturalistic methods [20]. In respect of the younger population, the majority of research has focussed on how lifestyle choices e.g. alcohol and recreational drug use might impact upon PM, with a general consensus that substance use impairs both subjective ratings [21] [22] and objective performance [23] even when subjective self-assessment records no decrements [24] [25]. However, little or no research has addressed the potential to improve performance on PM tasks, with that which has focussing on behavioural [26] and psychosocial interventions [27]. Given the lack of research in the area, the current study aims to assess the effects of *Salvia officinalis* and *Salvia lavandulaefolia* essential oil aromas on an objective video based measure of prospective memory performance.

2. Materials and Methods

2.1. Design

A single-blind, one factor, independent groups design was employed in this study. The independent variable was aroma condition and had three levels: *Salvia officinalis* aroma, *Salvia lavandulaefolia* aroma and no aroma (control). The dependent variables were Total, Event and Action scores from the video based prospective memory task. The overall sample size was calculated using G * Power and based on a power of 0.8 and an effect size of $f = 0.25$ calculated from previous aroma studies [13] [14] [16].

2.2. Participants

One hundred and thirty five healthy adult volunteers took part in the study. Recruitment took place through the automated participation pool provided by Sona-Systems Ltd. All volunteers were students in the School of Psychology and Sport Sciences at Northumbria University. All participants reported that they were non-smokers, had no history of respiratory disorders or decrements in their sense of smell. Participants were randomly allocated to the three conditions. The *Salvia officinalis* aroma condition was made up of 37 females (mean age = 21.3, SD = 3.6) and 8 males (mean age = 22.4, SD = 3.0). The *Salvia lavandulaefolia* aroma condition was made up of 36 females (mean age = 21.3, SD = 4.9) and 9 males (mean age = 23.1, SD = 3.8), and the control (no aroma) condition was made up of 36 females (mean age = 21.3, SD = 4.4) and 9 males (mean age = 23.9, SD = 4.4). Ethical approval for the study was obtained from the Department of Psychology Ethics Committee at Northumbria University.

2.3. Testing Cubicles

Testing cubicles measured 2.4 m long × 1.8 m wide × 2.4 m high and were maintained at a temperature of between 18 and 22 degrees Celsius throughout the testing sessions. The doors were kept closed except for participant access. Three identical cubicles were used and testing took place on three different days of the week (Monday, Wednesday, and Friday) to avoid cross contamination of aromas.

2.4. Aromas

The essential oils of *Salvia officinalis* and *Salvia lavandulaefolia* were used to provide the aromas. Both species were organically grown in Europe and were obtained from NHR organic essential oils, Brighton, UK. To diffuse the aroma, an "aroma stone" (Naturally thinking, Carshalton, Surrey, UK) was used. Five drops of the appropriate essential oil and 5 ml water were placed on the stone and left to diffuse into the testing cubicle, as a result of the constant temperature warming provided by the stone, for five minutes prior to testing each participant.

2.5. Prospective Memory Measures

Objective Prospective Memory (PM) was measured by the PRVP based on a methodology used by earlier researchers to study cannabis [28] and binge-drinking [24]. The PRVP involved presenting a list of 21 specific locations (e.g. "when you reach the store W. H. Smiths"), which were accompanied by a list of associated actions (e.g. "ask if there is a job available") which the respondent viewed for 1.5 minutes. This was immediately followed by a ten-minute video clip of a busy shopping area depicting a range of shop fronts and passers-by that provided location cues during which the previously presented location-action combinations were recalled (see

Table 1 for the full list of combinations). Before watching the video clip, the participant was instructed to remember each of the location-action pairings for later recall when viewing the video clip. The researcher ensured that the participant was aware that he/she should only write down each location-action combination on a blank response sheet when the familiar location was reached on viewing the video and not before. These instructions were given to ensure that the participant did not merely write down a list of location-action combinations at the start of the video clip, rather they recalled each combination as part of the ongoing PM task whilst monitoring the video clip. In addition to the main target locations, several other locations/occurrences were included which were not contained in the to-be-remembered list, acting as non-target distracter locations (e.g. passing other shop fronts, passers-by who talked to the camera). The inclusion of such was to ensure that the PM task was as similar to a more realistic PM scenario as possible [29]. One point was given for each location-action combination correctly recalled, ranging from 0 - 21 points per respondent, with the higher the score on the PRVP indicating the better one's PM is concluded to be. The PRVP has been used in previous research [24] [28] and shows good reliability ($\alpha = 0.68$).

2.6. Sensory Variables

Likert scales were used to assess participants' ratings of pleasantness and strength of ambient aromas. The scales ranged from 1 to 5 with higher values indicating stronger ratings of the variables.

2.7. Procedure

All testing took place on an individual basis between 9:00 and 12:00. Participants were informed that they were taking part in the validation of a testing system and no information was provided regarding the aromas prior to testing. Following the completion of a number of computerised tasks the video based prospective memory assessment began. To conclude the experiment the participants were fully debriefed and thanked for their time.

2.8. Results

Descriptive statistics for the dependent variables appear in **Table 2**. The data were analysed by way of one way independent groups ANOVAs using the statistical package SPSS 16 for windows. Significant results were followed up with Tukey post-hoc pairwise comparisons.

Table 1. A full list of the 18 event-action/memory combinations used on the PRVP.

Event	Action
When you reach the Halifax	Check if your loan has cleared
When you see 1st man pushing pushchair	Use mobile to text
When you see a woman sitting on a bench	Ask her the time
When you reach the store Dixons	Note how much "Play Station 2" costs
When you see girl sitting with dog	Note the colour of jacket of woman petting dog
At H Samuels	Buy a watch battery
At W H Smiths	Ask if any job available
At HMV	Buy an album
At Burger King	Buy a Milkshake
When you pass Flower Stall	Note the colour of stall's roof
At Wallis	Note how many Phone Boxes there are
At Thornton's	Buy bag of toffees
At the "Orange" shop	Buy a £10 top-up card
At Boots Store	Note what the boy is wearing on his face
At the mobile phone stall	Ask directions to station
At the Link	Note what instrument man is playing
When you meet a man asking for change	Check your pocket for 20 p
At the picture Stall	Note who the famous bear is

Table 2. Means (standard deviations) for the prospective memory video task.

	Total	Event	Action
S. officinalis	15.8 (5.3)	9.4 (2.4)	6.4 (3.2)
S. lavandulaefolia	14.5 (5.2)	8.8 (2.1)	5.7 (3.3)
Control	11.8 (2.9)	7.2 (1.4)	4.6 (2.1)

2.8.1. Prospective Remembering Video Procedure Total Score
The ANOVA identified significant differences between groups for the Total score on the PRVP $F(2,132) = 8.433$, $p < 0.001$, $\eta^2_{partial} = 0.113$. Tukey post hoc comparisons revealed both *Salvia officinalis* aroma (mean = 15.8) and *Salvia lavandulaefolia* aroma (mean = 14.5) conditions produced higher scores than the no aroma condition (mean = 11.9); $p < 0.001$ and = 0.020 respectively. The two aroma conditions did not differ significantly $p = 0.393$.

2.8.2. Prospective Remembering Video Procedure Event Score
The ANOVA identified significant differences between groups for the Event score on the PRVP $F(2,132) = 13.441$, $p < 0.001$, $\eta^2_{partial} = 0.169$. Tukey post hoc comparisons revealed both *Salvia officinalis* aroma (mean = 9.4) and *Salvia lavandulaefolia* aroma (mean = 8.8) conditions produced higher scores than the no aroma condition (mean = 7.2); $p < 0.001$ and = 0.001 respectively. The two aroma conditions did not differ significantly $p = 0.397$.

2.8.3. Prospective Remembering Video Procedure Action Score
The ANOVA identified significant differences between groups for the Action score on the PRVP $F(2,132) = 4.144$, $p = 0.018$, $\eta^2_{partial} = 0.059$. Tukey post hoc comparisons revealed that *Salvia officinalis* aroma (mean = 6.4) produced higher scores than the no aroma condition (mean = 4.6); $p = 0.014$. The *Salvia lavandulaefolia* aroma (mean = 5.7) conditions did not differ significantly to the SO or control condition, $p = 0.484$ and $p = 0.206$ respectively.

2.8.4. Pleasantness of the Aroma
The ANOVA identified significant differences between groups for the perceived pleasantness of the ambient aromas in the cubicles $F(2,132) = 4.683$, $p = 0.011$, $\eta^2_{partial} = 0.066$. Tukey post hoc comparisons revealed both *Salvia officinalis* aroma (mean = 3.8) and *Salvia lavandulaefolia* aroma (mean = 3.6) conditions were rated as more pleasant than the no aroma condition (mean = 3.0); $p = 0.039$ and 0.016 respectively. The two aroma conditions did not differ significantly $p = 0.942$.

2.8.5. Strength of the Aroma
The ANOVA identified significant differences between groups for the perceived intensity of the ambient aromas in the cubicles $F(2,132) = 20.207$, $p < 0.001$, $\eta^2_{partial} = 0.185$. Tukey post hoc comparisons revealed both *Salvia officinalis* aroma (mean = 3.7) and *Salvia lavandulaefolia* aroma (mean = 3.2) conditions were rated as more intense than the no aroma condition (mean = 2.0); $p < 0.001$ in both cases. The two aroma conditions did not differ significantly $p = 0.177$.

3. Discussion

Both *Salvia officinalis* and *Salvia lavandulaefolia* aromas produced a significant enhancement effect for the total scores on the video based prospective memory task. A more fine grained analysis of the scores revealed that this enhancement was restricted to "Event" based aspects of PM for *Salvia lavandulaefolia* aroma with no impact on action performance. In contrast, *Salvia officinalis* aroma significantly enhanced performance for both "Event" and "Action" based aspects of the task. The relationship between prospective memory and other forms of memory is something that engenders considerable debate [30], although there is some consensus that it may be seen as a separate and dissociable memory function [31]. As such, these findings provide interesting comparisons for effects on aspects of memory reported previously for both oral and aroma based administration of these herbs in

healthy young participants. With regard to SO, Tildesley found a significant improvement in the quality of memory factor and more specifically the secondary memory sub-factor, but not the working memory sub-factor, following a 666 mg dose of herbal extract when compared to the placebo control condition [9]. It has been argued that prospective memory only draws on working memory once the future event triggers an action. If the relationship were so, it might be predicted that SO aroma would not impact on the action measure of the task employed here. Given that this variable was enhanced by SO a more complex relationship might exist or indeed the systems serving PM performance might be distinct from working memory entirely. Interestingly however, in a study with a cohort of healthy elderly participants Scholey and colleagues reported much more striking effects following herbal SO administration [10]. As well as a positive effect on both secondary and working memory, the elderly also displayed an enhancement on the accuracy of attention factor. This may indicate that although perhaps not directly available for enhancement, working memory is open for the reversal of small decrements resultant of natural ageing. A study of the effects of aroma on prospective memory in the elderly may help elucidate the complex relationships between the different aspects of memory.

The significant difference found here between the SL aroma condition and the control condition for the "Event" scores might have been predicted based on previous research. Tildesley *et al.*, reported significant improvements in the quality of memory factor scores following oral administration of both SL herb and essential oil [11] [12]. Acetylcholinesterase inhibition has been proposed as one of the major reasons why an improvement in cognition is observed when SL essential oil is orally administered [11]. Savelev *et al.* performed an *in vitro* study which showed that eight terpenoid constituents of SL essential oil displayed acetylcholinesterase inhibitory properties [4]. Rusted, Ruest & Gray propose a mechanism by which compounds with cholinergic properties such as those found in extracts of *Salvia* sp. might enhance prospective memory [32]. Employing an event related fMRI procedure Rusted and colleagues demonstrated enhancements in prospective memory performance whilst concurrently completing an attention based task following nicotine administration. Such enhancements they argue are as a result of the cholinergic agonist properties of nicotine attenuating the attention drain that results from engaging with prospective memory tasks.

The effects reported here do not lend themselves to be easily explained by the hedonic valence mechanism. This mechanism suggests that the pleasantness of an aroma can impact on behaviour and emotional states [33], and some authors have reported that hedonic valence might also explain cognitive effects observed [34]. The two aromas employed here have distinctly different properties and effects, but were not rated differently in terms of pleasantness or strength. Similarly the differential effects found for aspects of prospective memory reported here do not lend themselves to explanation by the expectancy mechanism proposed by Howard and Hughes [35]. Although expectancy can be an important factor [36], it is unlikely that without expectancy manipulation the randomly allocated participants would have self-generated expectancies that produced the pattern outcomes observed.

Although the PRVP represents a useful method by which activities akin to everyday life can be tested in the laboratory, it does have its limitations that need to be considered by future researchers. A limitation of the current use of the PRVP is that it provided only a snapshot of everyday memory. As noted elsewhere [37] intentions are often carried out over prolonged delays (such as hours, or days, or weeks), whereas the present task was short in duration. Future research may wish to vary task duration, for example, comparing PRVP procedures that run for minutes with those running an hour (or more).

In order to further our understanding of herbs and herb-derived products such as essential oils, a number of practical approaches should be combined. The utilization of a single harvest source of herb to produce herbal and extract products for testing should be applied to allow accurate comparisons to be made in an area where standardised products do not exist. In addition *in vitro* analysis of pharmacological properties should be made to establish the levels of constituent compounds and their impact on neurotransmitter systems. Serum samples obtained from participants should be examined to assess if the active compounds have been absorbed, and to what extent following both oral ingestion and aroma exposure. If any active compounds are present in herb, essential oil and serum samples, and similar effects are observed for cognition and mood this would provide the strongest evidence yet that the mechanisms behind such effects are pharmacological.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Conflicts

There are no conflicts of interest (real or apparent) that may have a direct bearing on the subject matter of this article.

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