

Cognitive Processing

Cognitive strategy in verbal fluency: Sex differences, menstrual cycle, and menopause effects

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Corresponding Author:	Patricia E. Cowell, PhD The University of Sheffield Sheffield, UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND	
Corresponding Author Secondary Information:		
Corresponding Author's Institution:	The University of Sheffield	
Corresponding Author's Secondary Institution:		
First Author:	Patricia E. Cowell, PhD	
First Author Secondary Information:		
Order of Authors:	Patricia E. Cowell, PhD	
	Meghana Wadnerkar Kamble, PhD	
	Ramya Maitreyee, PhD	
	Rosemary A. Varley, PhD	
Order of Authors Secondary Information:		
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Cognitive strategy in verbal fluency: Sex differences, menstrual cycle, and menopause effects

Patricia E. Cowell^{1*†}, Meghana Wadnerkar Kamble^{2†}, Ramya Maitreyee^{1,3}, and Rosemary A. Varley⁴

¹School of Allied Health Professions, Nursing and Midwifery, University of Sheffield, Sheffield, UK

²School of Health Sciences, University of East Anglia, Norwich, UK

³Institute of Health Sciences, Bhubaneswar, India

⁴Division of Psychology and Language Sciences, University College London, London, UK

†These authors contributed equally to this work and share first authorship.

***Correspondence:**

Patricia E. Cowell

p.e.cowell@sheffield.ac.uk

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Abstract

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Keywords: verbal fluency, sex differences, menstrual cycle, menopause, cognitive strategy, language

Author Contributions

All authors contributed to study design and manuscript editing. XX, XX, and XX collected and analysed data. XX and XX wrote the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial, financial, or nonfinancial relationships that could be construed as a potential conflict of interest.

Ethical statement

All procedures involving human participants were performed in accordance with the ethical principles of the 1964 Declaration of Helsinki. Study protocols were approved by the

University of XX Research Ethics Review Panel, and participants provided informed written consent to take part.

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1 Introduction

The brain is both a target for and a source of sex hormones (Acaz-Fonseca et al. 2016; Lu et al. 2019; McEwen and Milner 2017; Zarate et al. 2017) with diverse impacts on human behaviour and cognition. Hormones exert their effects on neural systems across the lifespan, shaping behaviour and cognition through changes in gene expression (Calvo et al. 2016), neuronal function (Barth et al. 2015; Zarate et al. 2017), neural networks (Ali et al. 2018), and, in later life, neuroinflammation (Sarvari et al. 2012). In early life, hormones are involved in the early differentiation of female and male brains, and in the active feminisation and masculinisation of behaviour and cognition into adolescence. Hormones continue to shape neurocognitive structure and function across the adult years (Jacobs and Goldstein 2018; Rehbein et al. 2021; Ruehr et al. 2024), and have a critical role in sex differences in brain aging (Gurvich et al. 2018). In later life, estrogen, progesterone and testosterone impact neuronal (Zarate et al. 2017) and microglial (Nissen 2017) aging and neural disease progression. Thus, men and women show different patterns of healthy cognitive aging and decline (Gurvich et al. 2018; Levine et al. 2021; Matthews et al. 2016; McCarrey et al. 2016; Nebel et al. 2018; Rahman et al. 2019; Taylor et al. 2019). The neuroprotective effects of estrogen throughout adulthood have also been documented at the systems, synaptic, cellular and molecular levels (Zarate et al. 2017). In turn, these neuroprotective effects have been evaluated in relation to cortical aging and cognitive status in older adults (Kelly et al. 2008; Taylor et al. 2019).

Across the adult life span in women, naturally occurring changes in reproductive phases and stages allow for investigation of the dynamic interplay of hormonal and neurocognitive events. In adult women of reproductive age, the influence of hormones on the female brain, communicative behaviour and related cognitive function has been documented via human (Fernandez et al. 2003; Gurvich et al. 2018; Hamson et al. 2016; Kantarci et al. 2018; Kilpi et al. 2020; Reuben et al. 2021; Ryan et al. 2009; Weber et al. 2014) and animal models (Kelley et al. 2020; Tobiansky and Fuxjager 2020; Vahaba and Remage-Healey 2018). In terms of sex differences in humans, female advantages in the verbal domain are well documented (Barel and Tzischinsky 2018; Halpern and LaMay 2000; Hyde 2016; Yonker et al. 2003), and present a starting point from which to investigate the impact of ovarian hormones on speech and language abilities. Reproductive cycle models (e.g., menstrual and estrus) have been applied to capture the changes that occur over time in adult females from various mammalian species (Dubol et al. 2021; Souza et al. 2012; Sundström Poromaa and Gingnell 2014; Warren and Juraska 1997; Woolley and McEwen 1993). In humans, comparisons between menstrual cycle days that correspond to high or low ovarian hormone levels have revealed phasic effects on speech and language-based tasks (Scheuringer and Pletzer 2017; Wadnerkar et al. 2006; Whiteside et al. 2004). Some reports investigated changes in performance or ability associated with phase-specific hormone levels (Hampson 1990b, a; Mordecai et al. 2008; Rosenberg and Park 2002); whereas, others documented shifts in functional lateralisation (Cowell et al. 2011; Wadnerkar et al. 2008; Wong-Goodrich et al. 2020). Meta-analyses have shown significant, yet small, effect sizes for sex differences in verbal episodic memory, verbal fluency (Hirnstein et al. 2022; Hyde 2016) and dichotic listening (Voyer 2011). While not all studies report significant sex differences (Kheloui et al. 2023) or menstrual cycle effects (Pletzer et al. 2024; Sundström Poromaa and Gingnell 2014) in relation to verbal behaviours, evidence indicates that there may be a more consistent degree

1 of female advantage on neurocognitive systems that involve phonetic cueing in speech
2 perception and production (Sato 2020).

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4 Whilst gonadal hormones impact on differences in performance to varying degrees, inter-task
5 correlations also vary between the sexes (Cowell and Hugdahl 2000). This approach to
6 characterising the impact of hormones on behaviour and cognition via the associations among
7 tasks or task components, brings a neuropsychological element to the study of hormone
8 effects. By comparing patterns of correlations across the sexes and, importantly, within the
9 sexes across hormonal states or reproductive life stages (Cowell 2010), one can statistically
10 model and probe differences in functional organisation. Such correlational models can also
11 provide conceptual insight into cognitive networks (i.e., cross-task analysis) and cognitive
12 strategies (i.e., within-task component analysis).
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16 Verbal fluency is a multifactorial (Troyer et al. 1997), efficient and non-invasive test
17 (Melinder et al. 2005) commonly used in cognitive neuropsychological assessments
18 (Patterson 2011). Verbal fluency also has attributes that makes it an ideal measure of interest
19 in the study of cognitive ageing, cognitive strategy use, hormone effects and sex differences.
20 The verbal fluency test provides a brief observation of verbal functioning and is commonly
21 administered as a category/semantic (Benton 1968) or phonemic/letter-based task
22 (Newcombe 1969). Studies using verbal fluency to study sex and hormone effects have
23 typically used the letter-based fluency task, where participants are required to generate words
24 beginning with a particular letter in a given time span. Then, the total number of words
25 generated is used to assess word count, minus any repetitions and errors. An additional
26 scoring technique involves coding for specific retrieval patterns, namely cluster size and
27 number of switches made between clusters (Troyer et al. 1997). Clustering in the letter-based
28 task involves production of strings of words starting with the same letter combinations,
29 whereas switching involves search processes and cognitive set shifting to end clusters and
30 start new ones (Hirshorn and Thompson-Schill 2006; Rende et al. 2002; Temple 2002; Troyer
31 et al. 1997; Troyer et al. 1998a; Troyer et al. 1998b). The total words produced provides a
32 quantitative indicator of overall performance, whereas looking at the cluster size and number
33 of switches provides indicators of the underlying cognitive strategies employed in the fluency
34 task. In theory, efficient performance on the verbal fluency task involves optimisation of
35 clustering and/or switching.
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41 Verbal fluency has been used to demonstrate the effects of sex differences (Costa et al. 2014;
42 Hirnstein et al. 2022; Hyde 2016; Scheuringer and Pletzer 2017; Weiss et al. 2006), the
43 menstrual cycle (Hampson 1990a), the menopause (Berent-Spillson et al. 2012; Weber et al.
44 2014), and sex chromosome conditions such as Turner's Syndrome (Temple 2002). In these
45 studies, the letter-based verbal fluency task was a sensitive indicator of the hormonal impact
46 on cognition in women. However, in keeping with the larger literature on sex and hormone
47 effects on verbal abilities, not all reports on verbal fluency showed sex (Scheuringer and
48 Pletzer 2017; Sokołowski et al. 2020), menstrual phase (Pletzer et al. 2024; Sundström
49 Poromaa and Gingnell 2014), or menopause-associated hormone effects (Herlitz et al. 2007;
50 Kilpi et al. 2020; Kocoska-Maras et al. 2011). In relation to healthy ageing, the relative
51 stability of overall verbal fluency performance for the letter or phonemic version of the task
52 (Troyer et al. 1997), compared to its semantic fluency counterpart (Elgamal et al. 2011;
53 Maitreyee et al. 2023), confers its additional suitability for comparisons across age groups
54 where hormonally based effects are the focal design feature (Berent-Spillson et al. 2012). To
55 probe verbal fluency more deeply, analyses of clustering and switching may provide a more
56 sensitive set of measures for examining the effects of sex, reproductive hormones, and gender
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1 specific life stages on the cognitive strategies that underly performance. Strategy-based
2 differences between the sexes (Weiss et al. 2006) and across phases of the menstrual cycle
3 (Scheuringer and Pletzer 2017) have been previously studied by way of verbal fluency
4 clustering and switching and their neurofunctional correlates (Scheuringer et al. 2020). The
5 statistical relationships between total words generated and switching *versus* clustering
6 strategies have been studied in relation to healthy aging (Troyer et al. 1997) and, more
7 recently refined in the context of task- and sex-based effects (Scheuringer et al. 2017). We
8 extend this approach to women across menstrual cycle phases and menopausal stages in the
9 current research.

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11 Verbal fluency is subserved by lateralised frontotemporal systems. Frontal cortex including
12 the left inferior frontal gyrus is implicated in phonological processing, verbal working
13 memory (Costafreda et al. 2006) and the phonological demands required for letter-based
14 fluency (Baldo et al. 2006). The left frontal cortex is also implicated in motor-speech
15 behaviours (Bohland and Guenther 2006; Riecker et al. 2005). While switching is subserved
16 by the left frontal regions, clustering is subserved by the left temporal cortex (Hirshorn and
17 Thompson-Schill 2006; Rende et al. 2002; Troyer et al. 1997; Troyer et al. 1998a; Troyer et
18 al. 1998b). Moreover, the cortical regions linked to verbal fluency are reported to be sensitive
19 to estrogenic actions (Dietrich et al. 2001; Hamson et al. 2016; Kantarci et al. 2018) and
20 ageing effects (Heinzel et al. 2013; Kahlaoui et al. 2012). The sensitivity of the
21 neurocognitive systems that underpin verbal fluency, to the interactive effects of hormone
22 and age effects, further strengthens the case for conducting a detailed exploration of
23 clustering and switching strategies in relation to hormone phases and reproductive stages in
24 women.

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26 The current paper reports verbal fluency results of three studies from our laboratory, with a
27 focus on the profiles of underlying cognitive strategies in verbal fluency as compared
28 between: (a) men and women (ages 20-27 years), (b) women in different menstrual cycle
29 phases (ages 20-27 years) and (c) menopausal stages (ages 47-79 years). Combining data in
30 this way allowed for greater sample sizes and enabled comparisons that were central to
31 investigating the effects of ovarian hormones on women's cognitive processing as a function
32 of reproductive life stage. Traditional measures of verbal fluency performance such as total
33 words produced were investigated. In addition, a detailed examination of verbal fluency
34 strategies based on Troyer et al.'s (1997) clustering and switching was conducted.
35 Importantly, the relationships between clustering, switching and total word production were
36 compared across the sexes, and in women across menstrual cycle phases and menopausal
37 stages. The analysis was designed to uncover differences in the way hormones affect verbal
38 behaviour by how they influence its underlying cognitive organisation in healthy adult men
39 and women through a detailed comparison of correlation patterns between the sexes,
40 menstrual cycle phases, and menopausal stages. The study's primary objective was to
41 investigate verbal fluency performance in relation to the fluid cognitive processing abilities
42 that subserve rapid spoken word retrieval. This study specifically set out to investigate
43 cognitive verbal fluency strategy measures and their correlations with overall performance.
44 These involve clustering strategies in relation to lexical retrieval of word forms with common
45 orthographic/phonemic onsets and switching to different clusters, reflecting a higher order
46 executive function involved in breaking sets (i.e., abandoning a current form-based cluster
47 that has become unproductive, and moving to a new cluster). Thus, we posed the following
48 questions: i) how will the total word count be affected by sex differences, menstrual phases
49 and menopausal stages; ii) how will verbal fluency strategies, i.e., clustering and switching,
50 be affected by sex differences, menstrual phases and menopausal stages; and iii) what are the
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relationships between clustering, switching and total word production and do these relationships differ as a function of sex, menstrual phase and menopausal stage?

The study set out to test three hypotheses:

(i) Total word production would be greater in women compared to men, in women during the high hormonal phase compared to women during the low hormonal phase of the menstrual cycle, and in pre/perimenopausal women compared to post-menopausal women.

(ii) Total switches would be greater in women compared to men, in women during the high hormonal phase compared to women during the low hormonal phase of the menstrual cycle, and in pre/perimenopausal women compared to post-menopausal women.

It was also hypothesised that iii) total word production would be more highly correlated with number of switches in women compared to men, in women during the high hormonal phase compared to women during the low hormonal phase of the menstrual cycle, and in pre/perimenopausal women compared to post-menopausal women. This hypothesis was based on growing evidence for the role of ovarian hormones in women's executive function (Dunkin et al. 2005; Erickson et al. 2007; Navarro-Pardo et al. 2018; Sundström Poromaa and Gingnell 2014) which the current study sought to investigate via switching as an indicator of flexible cognitive processing in verbal fluency (Hamson et al. 2016).

2 Methods

2.1 Participants

The main methods and design features of the included studies are described below and summarised in Table 1.

Participants were healthy women (N=106) and men (N=20) with letter fluency data who volunteered for studies on sex differences, menstrual cycle and menopause effects on speech, language, and related behaviour. Participants were recruited from the University of XX student and staff population, as well as the local community, by means of posters, and email circulation. Background demographics, reproductive history, WASI Full IQ (FIQ) scores (Wechsler 1999), handedness, and verbal fluency measures were available for all participants.

Participants were native speakers of English with no known history of neurological, speech, language, or hearing difficulties. Women were not using oral contraceptives, HRT, or any hormone-based medications and had not been pregnant or lactating for a minimum of one year prior to the study.

FIQ was used as a measure of general cognitive ability. Handedness was used to confirm that the sample profiles were consistent with the wider population norms. This measure is salient given the relationship between handedness and neurocognitive organisation of language (Pujol et al. 1999) including verbal fluency in women (Cowell and Gurd 2018; Gurd et al. 2013). Assessment of FIQ and handedness enabled cross-study comparisons in relation to these sample characteristics.

Handedness was measured using a behavioural test battery of: (a) twenty items yielding scores between -40 (completely left-handed) and +40 (completely right-handed) in the sex difference and menstrual cycle studies (References have been blinded); and (b) ten items yielding scores between -100 (completely left-handed) and +100 (completely right-handed)

(Oldfield 1971) in the menopause study (references have been blinded). The majority of participants were rightwardly lateralised as represented by positive median scores (Table 1) Eighty-nine percent and eighty-six percent of participants from the ‘sex and menstrual cycle’ and menopause studies, respectively, had scores between +60% and +100%; this was consistent with the ranges documented in a recent meta-analysis of 200 handedness studies (Papadatou-Pastou et al. 2020).

Data were collected as part of a series of three studies between 2004 and 2016 that investigated the effects of sex, menstrual cyclicity, and menopause on speech, language, and related behaviour. Two studies investigated women longitudinally across menstrual cycle phases and one of these also included men (References have been blinded). Data from these two studies (Study 1, N=45: women, n=25, men, n=20; Study 2: women, N = 10, an age-matched subset from the total study) were combined into a single corpus of fifty-five participants for analysis of sex differences and menstrual cycle effects. A separate study investigated women (Study 3, N=71) from different menopause stages (references have been blinded). The verbal fluency data from the studies that investigated women longitudinally across the menstrual cycle and men, were not previously published in their entirety. Preliminary reports on performance and strategy for a subset of the data were presented in a conference abstract (reference has been blinded) and as part of a PhD thesis (reference has been blinded). The verbal fluency data from the study on women and menopause, were not previously published in their entirety. Preliminary reports on performance and strategy were presented in a conference abstract (reference has been blinded), as part of a PhD thesis (reference has been blinded) and for performance only in a subgroup of postmenopausal women (reference has been blinded). Thus, the current analysis reports new results on verbal fluency performance and strategy, for a larger set of combined data.

2.2 Procedures

To control for practice effects, the verbal fluency task was presented in a cross-sectional manner in all three studies. Women from repeated measures menstrual phase studies were tested on the verbal fluency task during only one of the phases. Women from the menopause study and men from the menstrual cycle and sex differences study were tested once.

The calendar method was used to classify the menstrual phases in both menstrual phase studies. The menstrual phase was defined as Days 2-5 and is known to have low levels of both estrogen (E) and progesterone (P), hence was classed as the Low E phase (LEP). An exception to this was that one LEP women was tested on day 6.

The periovulatory phase was defined as Days 8-11 and is known to have high levels of E and low levels of P.

The midluteal phase was defined as Days 18-25 and is known to have high levels of both E and P. Retrospective checks were conducted to corroborate that testing at Days 18-25 was during the midluteal phase. This was done by counting the number of days between testing and onset of the next menstrual cycle, which should be 14 days or less. In this sample (n=15) women in the midluteal phase at the time of verbal fluency testing had their next menstrual period within 3 to 13 days (mean = 7.67 days, SE = 0.0.74).

Only three women were tested during the periovulatory phase, therefore, women from both higher hormone phases were combined into a single group designated as the High E phase (HEP). This was done to maximise sample sizes for statistical comparison while maintaining a hormone-based distinction between groups.

1 Session 1 was counterbalanced across the menstrual phase to control for menstrual cycle
2 order impacts on the longitudinal measures. In addition, the time point for conducting the
3 single verbal fluency test was counterbalanced across sessions 1 and 2 for the sex and two-
4 phase menstrual study and across sessions 1, 2, and 3 for the three-phase menstrual cycle
5 study. The resulting breakdown for the current sample is as follows: (a) VF was tested at the
6 LEP for n=17 women. Of these, VF was tested at the LEP during session 1 for n=9 women,
7 and VF was tested at the LEP during session 2 for n=8 women; (b) VF was tested at the HEP
8 for n=18 women. Of these, VF was tested at the HEP during session 1 for n=12 women, and
9 VF was tested at the HEP during session 2 for n=6 women.

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11 The mean menstrual cycle length for all women in the combined menstrual cycle dataset was
12 29.16 days, SE=0.43 (minimum=23 and maximum=35 days).

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14 Classifications in relation to menopausal stages were designated for women in the menopause
15 study (Table 1). Premenopausal women reported having monthly cycles, but with some subtle
16 changes in flow volume and cycle duration. Perimenopausal women reported having irregular
17 cycles with delays in onset and occurrence. Women in the pre- and peri-menopausal stages
18 were combined into a single group, based on their status of not having met the post-
19 menopausal criteria. Post-menopausal women whose menses had paused for at least one year
20 formed a second group. Definitions of menopause stages used to classify women's status
21 were based on verbal reports, followed published guidelines (Harlow et al. 2012; WHO 1996)
22 and are summarised in Table 1. All postmenopausal women had attained natural menopause
23 after the age of 40; those with hysterectomy alone or hysterectomy with unilateral/bilateral
24 oophorectomy were excluded (Harlow et al. 2012; Jewelewicz and Schwartz 1986; Laughlin
25 and Thorney Croft 2003).

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Table 1. Designs used in the current report, plus summary statistics for sex, age, hormone status, handedness and FIQ for the two datasets. (SE standard error; HEP High estrogen phase; LEP low estrogen phase; *one woman in this group was tested on day 6). See Methods for details of the two scales used to assess handedness.

Study Design and Comparisons	Age range Mean (SE)	Women’s hormone status expressed as testing day of menstrual cycle or menopause stage	Handedness Median (range)	FIQ Range Mean (SE)
<p>Menstrual cycle and sex differences N=55</p> <p>Sex: Male vs. Female Cycle Phase: Menstrual vs. Perioovulatory/Midluteal</p> <p>HEP Women n=18 LEP Women n=17 Men n=20</p>	<p>20-27years, M=22.58 (0.27)</p> <p>HEP Women: 23.22 (0.47) LEP Women: 22.41 (0.56) Men: 22.15 (0.38)</p> <p>F(2, 52) = 1.452, n.s.</p>	<p>Days of testing, Mean (SE)</p> <p>HEP Women, Day 8-25, 18.94 (1.25) LEP Women*, Day 2-5, 4.06 (0.26)</p>	<p>All: +34 (+8 to +40)</p> <p>HEP Women: +32 (+8 to +38) LEP Women: +35 (+12 to +40) Men: +34 (+28 to +39)</p>	<p>All: 103-138 119.67 (1.13)</p> <p>HEP Women: 119.83 (2.24) LEP Women: 116.71 (1.88) Men: 122.05 (1.66)</p> <p>F(2, 52)=1.93, n.s.</p>
<p>Menopause N=71</p> <p>Menopause stage: Pre/Perimenopausal vs Postmenopausal Women</p> <p>Pre- and Perimenopause n=19 Postmenopause n=52</p>	<p>47-79 years Mean=60.08 (1.14)</p> <p>Pre- and Perimenopause Women, 47-55 years: 50.32 (0.44)</p> <p>Postmenopause women 48-79 years: 63.65 (1.21)</p> <p>F(1,69)=43.36, p<0.001</p>	<p>Premenopause: monthly cycles, but with subtle changes in flow and cycle length.</p> <p>Perimenopause: irregular cycles with delays in occurrence.</p> <p>Postmenopause: permanent cessation of menstruation for at least 12 consecutive months.</p>	<p>All: +100 (-100 to +100)</p> <p>Pre- and Perimenopause Women: +90 (-100 to +100)</p> <p>Postmenopause Women: +100 (-100 to +100)</p>	<p>All: 103-132 120.63 (0.85)</p> <p>Pre- and Perimenopause Women: 118.37 (1.69)</p> <p>Postmenopause Women: 121.46 (0.97)</p> <p>F(1,69)=2.66, n.s.</p>

2.2.1 Verbal fluency data collection and scoring

The letter based verbal fluency task requires participants to produce as many words as possible beginning with letters F, A, and S in a time span of one minute, for a total of three one-minute trials per person. Participants were instructed not to produce proper names or morphological variants of the same word (e.g., sleep, sleeping).

Testing was done in a quiet room. Responses were recorded onto a digital recorder (Marantz Portable Professional Solid State Recorder, Model PMD670) using a sampling rate of 44100 Hz. Audio files were then transferred onto Adobe Audition (version 1.5, Adobe Systems Incorporated) (menstrual cycle and sex difference data) or Praat software (Boersma 2001; Boersma and Weenink 2023) (menopause data) for later transcription. The audio files were stored as PCM .wav files.

Three scores were calculated for each letter trial. These included the total number of correct words generated (excluding errors and repetitions), mean cluster size and the number of switches (Troyer et al., 1997). Clusters were defined as groups of consecutively generated words that began with the same first two letters (e.g., about, abyss), words that differed only by a vowel (e.g., fit, fat, foot), words that rhymed (e.g., sand, stand), or were homophones (e.g., sun, son). Words were classified as homophones if clarified by the participant during word production, by defining or spelling the words aloud. The cluster size was calculated beginning with the second word in each cluster. Thus, a cluster with two words got a score of one; a cluster with three words got a score of two and so on. Switches were calculated as the total number of transitions between clusters, including single words for each of the trials. Errors and repetitions were removed from total word counts but were included in calculations of cluster size and switching (Troyer et al. 1997). Total words, number of switches and mean cluster size were computed within each letter trial for use in analyses conducted as a function of the variable Letter; the individual letter values were averaged across the three letter trials for use in tables and analyses that were not conducted as a function of Letter.

2.2.2 Inter-rater reliability

Raters were either authors (XX, XX, XX) or doctoral students with linguistics backgrounds (XX, XX – see Acknowledgements) from the University of XX. Inter-rater reliability checks were conducted within each of the three studies that contributed data to the current investigation. Pearson's correlations were used to assess inter-rater reliability, along with intraclass correlation coefficients (ICCs). Correlation values for all three studies are provided in the supplementary material (Supplementary Table 1).

For the first menstrual cycle and sex differences study, an independent rater (XX) listened to the original audio files and re-scored the data according to the methods applied by the first rater (XX) for all 45 participants. Within letter, all but one measure achieved reliability above 0.90 (the exception was mean cluster size for the letter S, $r=0.89$). Across letters for the whole of the verbal fluency task, all measures achieved reliability above 0.94.

Given the high reproducibility of the method across raters, a sampling method was used to ascertain inter-rater reliability in the other two studies. For the second menstrual cycle study, data for 12 participants were scored by two raters (XX, XX). Within letter, all but one measure achieved reliability above 0.90 (the exception was mean cluster size for the letter S,

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$r=0.79$). Across letters for the whole of the verbal fluency task, all measures achieved reliability above 0.93.

Similarly, for the menopause study, data for 8 participants were scored by two raters (XX, XX). Within letter reliability above 0.93 was achieved for all but one measure (the exception was switches for the letter S, $r=0.87$). Across letters, all measures achieved reliability above 0.97.

2.2.3 Design and Data-Analysis

Preliminary analyses included comparisons of FIQ to confirm between-group comparability. The verbal fluency task was administered cross-sectionally, therefore, the FIQ scores were analysed to rule out any differences in intellectual ability estimates between women at the HEP and LEP phases and men, and between women across the two menopause stages. Results of FIQ ANOVAs are reported in Table 1 and revealed no significant differences between groups.

The original studies of younger adults were powered mainly to detect repeated measures effects across the menstrual cycle within women in the domains of speech production and speech perception. For those measures of interest, medium effect sizes were estimated from existing two-phase menstrual cycle data for the acoustic phonetic measure of voice onset time, and for dichotic listening speech perception scores. The decision to pool the data to achieve a larger combined sample for verbal fluency analysis in the current paper was taken to enable larger datasets for a cross-sectional menstrual cycle comparison. Moreover, it was decided to publish the data from the younger participants together with the data from the older pre/peri- and postmenopausal women to further expand the size of the overall data set and its representation across the reproductive lifespan. Thus, the power analysis for the current study was conducted after joining the smaller datasets from the younger participant groups. These power analyses (presented below) were therefore conducted prior to the combined data analysis, not prior to the study design, for the reasons outlined above. Conducting power analyses for the ANOVAs, together with the reporting of partial eta squared scores from the ANOVA effects, provides the statistical information needed to understand the current results in the context of type II ($\beta=0.20$) and type I ($\alpha=0.05$) error probabilities. For consistency and internal comparison purposes, this approach was applied to the menopause dataset.

In the current study, the analytic objective of the main analyses was to examine effects of menstrual cyclicity, sex differences, and menopause on verbal fluency as a performance measure and on the underlying cognitive strategies. Separate repeated measures ANOVAs were conducted to examine differences at the Group level as the between-subjects factor, where the Groups were defined by sex, menstrual phases, and menopausal stages, and at the task level with Letter (F, A, S) as the within-subjects factor. Total words, mean cluster size and total switches were the dependent measures. Power estimates for these analyses were computed using G*Power software (Faul et al. 2009; Faul et al. 2007) and are summarised below in relation to medium and large effect sizes (Cohen 1977; Richardson 2011). Further details of analyses conducted for each comparison are presented in the supplementary material.

Estimates of sample size to achieve 80% statistical power for medium effect sizes ($f = 0.25$, $\eta_p^2 > 0.0588$) in repeated measures ANOVAs ($\alpha = 0.05$, $k = 2$, repeated measures = 3, correlation among repeated measures = 0.330, and $\epsilon = 0.996$) was $N=72$ for between factor effects and $N=38$ for within factor effects and interactions of within and between factors. An $N=30$ for between factor effects and $N=16$ for within factor effects and interactions of within and between factors would be required to achieve 80% power for large effects sizes ($f = 0.40$, $\eta_p^2 > 0.1379$). Thus, with the sample sizes of the current datasets, the

models were sufficiently powered for medium to large effects from the menopause analysis (N=71) and elements of the sex difference analysis (N=55). The models were sufficiently powered for large effects from the menstrual cycle analysis (N=35).

Pearson's correlations were used to analyse the inter-relationships between the total words produced, cluster size and number of switches. This was done separately for men and groups of women as defined by menstrual cycle phases or menopause stages.

3 Results and interim summaries

See Table 2 for verbal fluency means (SEs) for total words, number of switches, and mean cluster size, and Table 3 for correlations among these three measures, as a function of sex, menstrual cycle phase, and menopausal stage.

3.1 Sex differences and menstrual cycle phase effects.

3.1.1 Repeated measures analyses

In relation to the above stated hypotheses, comparisons of participants aged 20-27 years were conducted: (a) by sex (comparing all women to men); and (b) by menstrual phase (comparing women in the LEP to those in the HEP group).

ANOVAs with Group (Women n=35, Men n=20) as the between group factor and Letter (F, A, S) as the within-subjects factor were conducted for total words, mean cluster size and number of switches.

Total words: Letter was significant ($F=31.95$, $d.f.=2,106$, $p<0.001$, $\eta_p^2=0.376$) but Group ($F=0.10$, $d.f.=1,53$, $n.s.$, $\eta_p^2=0.002$) and Letter x Group ($F=0.60$, $d.f.=2,106$, $n.s.$, $\eta_p^2=0.011$) were not. Post-hoc comparisons for Letter showed that effects were based on more words for S (mean = 18.76, SE = 0.56) compared to F (mean = 16.09, SE = 0.71) compared to A (mean = 13.42, SE = 0.56) ($S>F$, $t(54\text{ d.f.}) = 4.96$, $p<0.001$; $S>A$, $t(54\text{ d.f.}) = 8.23$, $p<0.001$; $F>A$, $t(54\text{ d.f.}) = 4.01$, $p<0.001$); the significance of all three post-hoc comparisons survived Bonferroni adjustment ($p < 0.017$).

Mean cluster size: Letter ($F=4.38$, $df=2,106$, $p<0.01$, $\eta_p^2=0.076$) was significant, but Group ($F=0.85$, $d.f.=1,53$, $n.s.$, $\eta_p^2=0.016$) and Letter x Group ($F=2.50$, $d.f.=2,106$, $n.s.$, $\eta_p^2=0.045$) were not. Post-hoc comparisons for Letter showed that effects were based on larger mean cluster sizes for F (mean = 1.46, SE = 0.10) compared to S (mean = 1.39, SE = 0.09) and A (mean = 1.18, SE = 0.09). Of these three comparisons, only the $F>A$ contrast was significant ($F>A$, $t(54\text{ d.f.}) = 2.46$, $p=0.017$), but it did not survive Bonferroni adjustment ($p < 0.017$).

Total switches: Letter ($F=3.62$, $df=2,106$, $p<0.05$, $\eta_p^2=0.064$) was significant, but Group ($F=0.93$, $d.f.=1,53$, $n.s.$, $\eta_p^2=0.017$) and Letter x Group ($F=0.04$, $d.f.=2,106$, $n.s.$, $\eta_p^2=0.001$) were not. Post-hoc comparisons for Letter showed that effects were based on more switches for S (mean = 4.60, SE = 0.51) compared to F (mean = 3.55, SE = 0.50) compared to A (mean = 2.96, SE = 0.42). Of these three comparisons, only the $S>A$ contrast was significant ($S>A$, $t(54\text{ d.f.}) = 2.84$, $p=0.006$), and it did survive Bonferroni adjustment ($p < 0.017$).

1 ANOVAs with Group (HEP Women n=18, LEP Women n=17) as the between group factor
2 and Letter (F, A, S) as the within-subjects factor were conducted for total words, mean cluster
3 size and number of switches.

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5 Total words: Letter ($F=24.28$, $d.f.=2,66$, $p<0.001$, $\eta_p^2=0.424$) was significant, but Group
6 ($F=4.02$, $d.f.=1,33$, $n.s.$, $\eta_p^2=0.109$) and Letter x Group ($F=0.04$, $d.f.=2,66$, $n.s.$, $\eta_p^2=0.001$)
7 were not significant. Post-hoc comparisons for Letter showed that effects were based on more
8 words for S (mean = 18.80, SE = 0.78) compared to F (mean = 16.11, SE = 0.98) compared
9 to A (mean = 13.00, SE = 0.76) ($S>F$, $t(34\text{ d.f.}) = 4.11$, $p<0.001$; $S>A$, $t(34\text{ d.f.}) = 6.50$,
10 $p<0.001$; $F>A$, $t(34\text{ d.f.}) = 3.49$, $p<0.001$); the significance of all three post-hoc comparisons
11 survived Bonferroni adjustment ($p < 0.017$).
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13

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15 Mean cluster size: Letter was not significant ($F=0.18$, $d.f.=2,66$, $n.s.$, $\eta_p^2=0.005$). Group
16 ($F=4.78$, $df=1,33$, $p=0.036$, $\eta_p^2=0.126$) was significant with women at the HEP ($M=1.57$,
17 $SD=0.51$) having larger mean cluster sizes than women at the LEP phase ($M=1.20$, $SD=0.48$)
18 ($ES\ d = 0.747$). Letter x Group ($F=0.24$, $d.f.=2,66$, $n.s.$, $\eta_p^2=0.007$) was not significant.
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22 Total switches: Letter was not significant ($F=2.78$, $d.f.=2,66$, $n.s.$, $\eta_p^2=0.078$). Group
23 ($F=4.78$, $df=1,33$, $p=0.036$, $\eta_p^2=0.127$) was significant with women at the HEP ($M=4.89$,
24 $SD=2.81$) producing more switches than women at the LEP phase ($M=2.96$, $SD=2.38$) ($ES\ d$
25 $= 0.741$). Letter x Group ($F=0.24$, $d.f.=2,66$, $n.s.$, $\eta_p^2=0.007$) was not significant.
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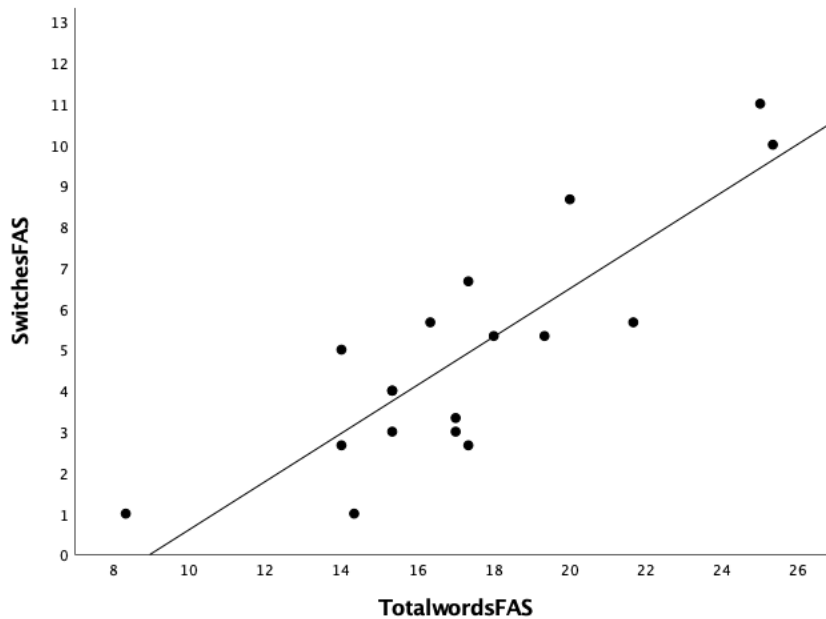
28 **3.1.2 Correlational analysis**

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30 There were no significant Letter x Group effects, therefore the data were pooled by averaging
31 across Letter for correlation analysis. ANOVA results showed significant effects related to
32 menstrual cycle phase, therefore, women's data were analysed separately for the HEP and
33 LEP groups. Pearson correlations were computed within each group and compared across the
34 three groups to examine relationships between total words, number of switches and mean
35 cluster size and are presented in Table 3.
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38
39 In participants aged 20-27 years, both HEP and LEP women had significant correlations
40 between switches and total words that were larger in magnitude compared to men. In
41 contrast, women at the LEP phase and men had significant correlations between cluster size
42 and total words that were larger in magnitude compared to women at the HEP phase. A
43 similar pattern was observed for the correlations between switches and mean cluster size, but
44 without significant correlations for any group. Group differences in correlations were
45 significant for 'total words to switches' between HEP women and men (Fisher's $z = 2.35$,
46 two-tailed $p = 0.019$). No other between group contrasts were statistically significant for
47 correlations in 'total words to switches' or 'total words to cluster size.' The correlation
48 between total words and switches for HEP women is depicted in Figure 1. Fisher-z
49 comparisons are summarised in Table 4.
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54 Spearman's correlations were also conducted to confirm the robustness of the above
55 associations given the degree of naturally occurring variability at the high and low ends of
56 some within-group distributions (See Figure 2). These aligned closely with the Pearson's
57 correlations (Table 3).
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Figure 1. Correlation between number of switches and total words in women at HEP with regression line for $r=0.848$ ($p<0.001$). (SwitchesFAS = number of switches, TotalwordsFAS = total number of words).



3.1.3 Interim summary

For sex differences, there were no statistically significant main or interaction effects for Sex. In that context, only the mean value difference for the number of switches was in the predicted direction (Women, $n=35$, mean = 3.95, SE = 0.46; Men, $n=20$, mean=3.27, SE = 0.48). Although not predicted, non-significant trends for mean cluster size also followed this pattern (Women, $n=35$, mean = 1.39, SE = 0.09; Men mean=1.26, SE = 0.09). A non-significant pattern in the direction opposite to predictions was observed in total words (Women, $n=35$, mean = 15.97, SE = 0.70; Men mean=16.30, SE=0.63).

Stronger support for the hypotheses was observed with the menstrual phase comparisons between women which showed a significantly higher number of switches and a non-significant trend for more words in the HEP group. In addition, mean cluster size was significantly larger in HEP women. (See Table 2 for means)

With respect to the task, Letter based differences were significant for all sex-based analyses with the pattern of $S \geq F > A$ for number of words, mean cluster size and number of switches. Between women, letter based differences showed the same $S \geq F > A$ pattern which was significant only for total words. Thus, letter based effects were more evident for total words than to cluster size and switches.

Results from the correlations supported the hypothesis that total words would be more highly correlated with number of switches in women compared to men. The prediction that switches would be more strongly associated with the menstrual cycle HEP than the LEP was also supported. Indeed, the HEP women had a significantly higher correlation than the men. Another key distinction between cycle phase x sex groups was observed between total words

1 and cluster size, where HEP women showed lower correlations compared to LEP women and
2 men.

3
4 The new finding from this study was that the profiles of correlations between strategy-based
5 measures (clusters *versus* switches) and total words differed depending on sex and cycle
6 phase. Women at the HEP maximised their word count with switching more than clustering
7 behaviours. The contrast between the two correlations (Total words and switches, $r=0.848$;
8 Total words and cluster size, $r=0.052$) was distinct among the three young adult groups.
9 Women at the LEP used both strategies with a more balanced combination of switching and
10 cluster size. Men maximised their word count by using larger clusters. Table 5 presents these
11 effects by the rank order of correlations between total words and switches; this highlights the
12 relationships between switching and cluster size correlations across the groups in a series of
13 directional comparisons between strategy types.
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15

16 3.2 Menopause effects

17 3.2.1 Repeated measures analysis

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19 ANOVAs with Group (Pre/Perimenopause $n=19$, Postmenopause $n=52$) as the between factor
20 and Letter (F, A, S) as the within-subjects factor were conducted for total words, mean cluster
21 size and number of switches. Given the span of ages within and across the groups (see Table
22 1), Age as a correlate to verbal fluency measures was examined prior to analysis to determine
23 the need for covariance in the model.
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25

26
27 Total words: Age did not correlate significantly with letter fluency for individual letters or
28 across all letters for total words within groups (all letters: pre/perimenopause: $r=0.35$, *n.s.*;
29 postmenopause, $r=-0.19$, *n.s.*) or across groups (all letters: $r=-0.18$, *n.s.*), so was not added as
30 a covariate to the ANOVA.
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34 Letter was significant ($F=18.47$, $d.f.=2,138$, $p<0.001$, $\eta_p^2=0.211$) but Group ($F=0.65$,
35 $d.f.=1,69$, *n.s.*, $\eta_p^2=0.009$) and Letter x Group ($F=0.29$, $d.f.=2,138$, *n.s.*, $\eta_p^2=0.004$) were not.
36 Post-hoc comparisons for Letter showed that effects were based on more words for S (mean =
37 19.28, SE = 0.59) compared to F (mean = 16.35, SE = 0.60) and A (mean = 15.56 SE = 0.62);
38 two of these post-hoc comparisons were significant (S>F, $t(70 \text{ d.f.}) = 5.55$, $p<0.001$; S>A, t
39 ($70 \text{ d.f.}) = 6.16$, $p<0.001$) and both survived Bonferroni adjustment ($p < 0.017$).
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44 Mean cluster size: Age did not correlate significantly with letter fluency for individual letters
45 or across all letters for mean cluster size within groups (all letters: pre/perimenopause:
46 $r=0.10$, *n.s.*; postmenopause, $r=0.03$, *n.s.*) or across groups (all letters: $r=-0.02$, *n.s.*), so was
47 not added as a covariate to the ANOVA.
48
49

50 Letter was significant ($F=4.51$, $d.f.=2,138$, $p<0.05$, $\eta_p^2=0.061$) but Group ($F=0.31$, $d.f.=1,69$,
51 *n.s.*, $\eta_p^2=0.004$) and Letter x Group ($F=1.35$, $d.f.=2,138$, *n.s.*, $\eta_p^2=0.019$) were not. Post-hoc
52 comparisons for Letter showed that effects were based on more words for S (mean = 1.66, SE
53 = 0.07) and F (mean = 1.61, SE = 0.08) compared to A (mean = 1.32, SE = 0.07); ; two of
54 these post-hoc comparisons were significant (S>A, $t(70 \text{ d.f.}) = 3.71$, $p<0.001$; F>A, $t(70$
55 $d.f.) = 2.85$, $p<0.01$) and both survived Bonferroni adjustment ($p < 0.017$).
56
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59 Total switches: Age did not correlate significantly with letter fluency for individual letters or
60 across all letters for switches within groups (all letters: pre/perimenopause: $r=0.12$, *n.s.*;
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1 postmenopause, $r=0.06$, n.s.) or across groups (all letters: $r=0.003$, n.s.), so was not added as
2 a covariate to the ANOVA.

3 Letter ($F=1.69$, d.f.=2,138, n.s., $\eta_p^2=0.024$), Group ($F=0.38$, d.f.=1,69, n.s., $\eta_p^2=0.005$) and
4 Letter x Group ($F=0.60$, d.f.=2,138, n.s., $\eta_p^2=0.009$) were not significant.
5
6

7 **3.2.2 Correlational analysis**

8
9 There were no significant Letter x Menopause effects, therefore the data were pooled across
10 Letter for correlation analysis. Pearson correlations were computed within each group and
11 compared across menopause groups to examine relationships between total words, number of
12 switches and mean cluster size.
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16 Both groups showed moderate correlation coefficients between switches and total words and
17 between cluster size and total words (Table 3) which were significant in the postmenopausal
18 group.
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20
21 Women in the pre/perimenopausal group had similar non-significant correlation coefficients
22 between switches and clusters with total words. In contrast, women in the postmenopausal
23 group showed a slightly stronger correlation between total words and mean cluster size.
24

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26 Comparisons between pre/perimenopausal and postmenopausal women for ‘total words to
27 switches’ and ‘total words to cluster size’ were not statistically significant.
28

29
30 Spearman’s correlations were also conducted to confirm the robustness of the above
31 associations given the degree of naturally occurring variability at the high and low ends of
32 some within-group distributions (See Figure 2). These aligned closely with the Pearson’s
33 correlations (Table 3).
34

35 **3.2.3 Interim summary**

36
37 There were no statistically significant Group or Group x Letter effects. However, the non-
38 significant trends in the mean values followed the predicted pattern of women in the pre/peri
39 menopause stage generating more words and making more switches compared to women in
40 the postmenopausal stage. A similar pattern of means was observed with cluster size.
41
42

43
44 With respect to the task, Letter was significant for the total words produced and mean cluster
45 size showing the same $S \geq F > A$ pattern observed for the sex and menstrual cycle phase
46 analyses.
47

48
49 Correlations between strategy-based measures (switches *versus* cluster size) with total words
50 did not differ markedly depending on the menopausal stage. Due to a smaller sample size,
51 correlations in women at the pre/perimenopause were not significant. However, women in
52 both pre/perimenopause and postmenopause stages showed moderate correlation coefficient
53 magnitudes with both switching (0.437, 0.408) and clustering (0.431, 0.506) to total word
54 count. However, there was a tendency for switching to correlate less, and for cluster size to
55 correlate more, with total word count in the postmenopause group. Table 5 presents these
56 effects by the rank order of correlations between total words and switches; this highlights the
57 relationships between switching and cluster size correlations across the pre/peri- and
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postmenopause groups and positions their correlation patterns between those of LEP women and men.

Table 2. Means (SEs) for total words, mean cluster size and total switches as a function of menstrual phase, sex, and menopause stage across the studies. Values are averaged across the letters F, A, and S.

	FAS Total Words	FAS Mean Cluster Size	FAS Total Switches
Menstrual cycle phases in women and men			
HEP Women n=18	17.28 (0.95)	1.57 (0.12)	4.89 (0.66)
LEP Women n=17	14.59 (0.94)	1.20 (0.12)	2.96 (0.58)
Men n=20	16.30 (0.63)	1.26 (0.09)	3.27 (0.48)
Menopause stages			
Pre/Perimenopause Women n=19	17.75 (0.81)	1.58 (0.09)	3.77 (0.39)
Postmenopause Women n=52	16.81 (0.64)	1.51 (0.06)	3.43 (0.30)

Table 3. Correlation analyses [95% Confidence Intervals] with large effect sizes ($r > 0.50$) indicated in bold (Cohen 1992) (* $p < 0.05$; ** $p < 0.01$). Confidence intervals were bias corrected, accelerated, and computed using 1000 bootstrap samples. Pearson correlations that survived Bonferroni corrections for multiple comparisons $p < 0.05/5 = p < .01$ are underlined. *Spearman's rank correlation coefficients [95% Confidence Intervals] are provided in italics.*

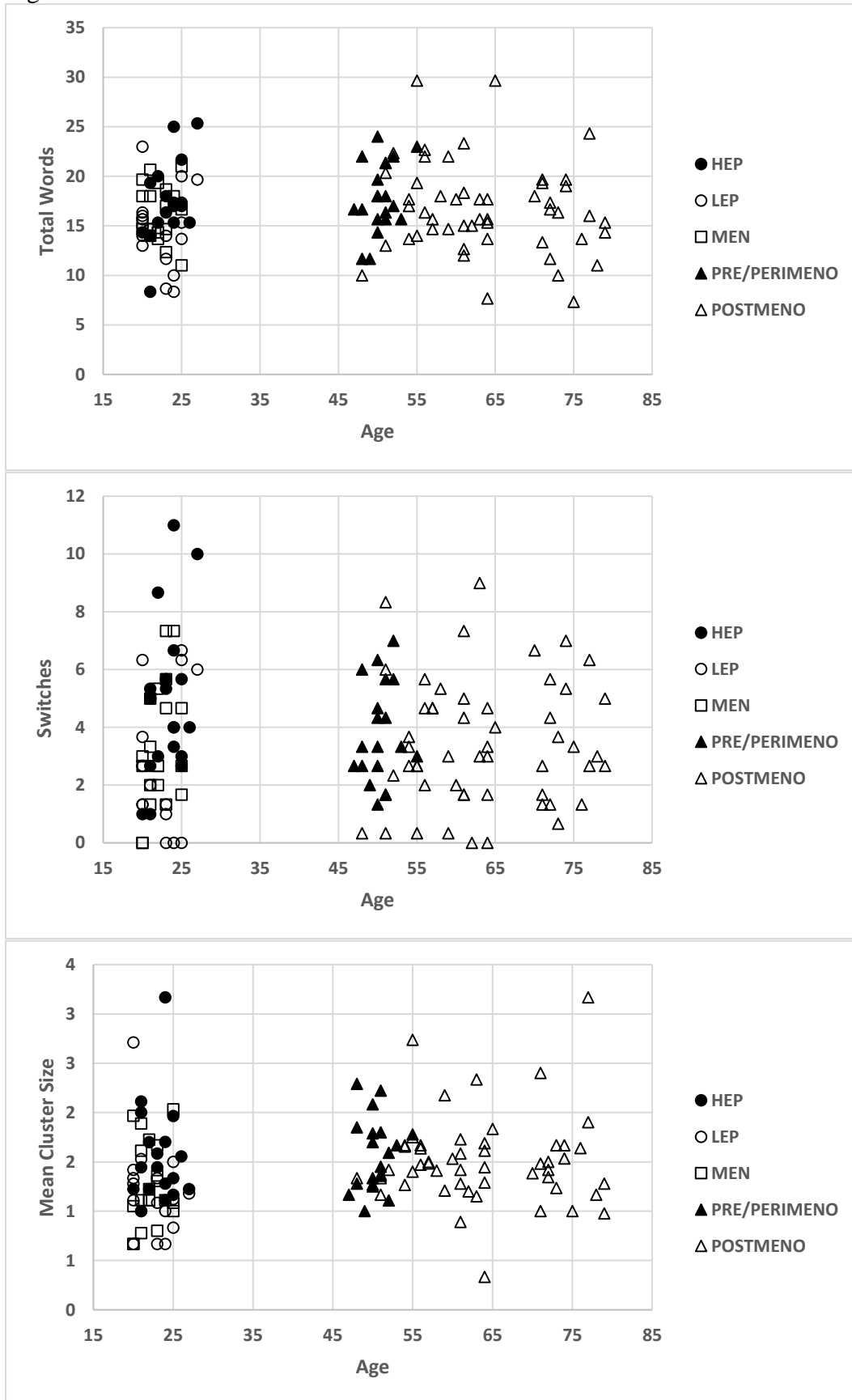
	Total words & Switches	Total words & mean cluster size	Switches & mean cluster size
Menstrual cycle phases in women and men			
HEP Women n=18	<u>0.848</u>** [0.625, 0.938] p<0.001 <i>0.768**</i> [0.458, 0.912]	0.052 [-0.382, 0.503] p=0.837 <i>-0.016</i> [-0.491, 0.466]	-0.036 [-0.498, 0.564] p=0.886 <i>0.162</i> [-0.343, 0.594]
LEP Women n=17	<u>0.577</u>* [0.212, 0.825] p<0.015 <i>0.650**</i> [0.232, 0.866]	<u>0.639</u>** [0.094, 0.845] p=0.006 <i>0.443</i> [-0.064, 0.768]	0.331 [0.008, 0.793] p=0.195 <i>0.436</i> [-0.072, 0.764]
Men n=20	0.400 [0.012, 0.728] p=0.080 <i>0.369</i> [-0.102, 0.705]	<u>0.612</u>** [0.214, 0.840] p=0.004 <i>0.530*</i> [0.100, 0.793]	0.435 [-0.049, 0.876] p=0.055 <i>0.599**</i> [0.199, 0.828]
Menopause stages			
Pre/Perimenopause Women n=19	0.437 [0.027, 0.750] p=0.061 <i>0.358</i> [-0.129, 0.706]	0.431 [0.074, 0.757] p=0.065 <i>0.468*</i> [0.003, 0.767]	0.101 [-0.362, 0.502] p=0.680 <i>0.109</i> [-0.376, 0.547]
Postmenopause Women n=52	<u>0.408</u>** [0.175, 0.618] p=0.003 <i>0.474**</i> [0.223, 0.666]	<u>0.506</u>** [0.211, 0.756] p<0.001 <i>0.495**</i> [0.249, 0.681]	-0.057 [-0.294, 0.199] p=0.686 <i>-0.052</i> [-0.327, 0.232]

Table 4. Fisher’s z-score comparisons of between group correlations. Comparisons are summarised by rank for those yielding significant differences, up to and including the nearest threshold for non-significant contrast. The comparison that survived Bonferroni correction for multiple comparisons $p < 0.05/4 = p = 0.0125$) is underlined.

Total words and Switches	Fisher's z	p-values two-tailed
HEP vs Postmenopause	<u>2.78</u>	<u>0.005</u>
HEP vs Men	2.35	0.019
HEP vs Pre/PeriMeno	2.20	0.028
HEP vs LEP	1.61	0.105
Total words and mean cluster size	Fisher's z	p-values two-tailed
HEP vs LEP	1.91	0.056
HEP vs Men	1.86	0.063
HEP vs Postmenopause	1.71	0.087
HEP vs Pre/PeriMeno	1.14	0.254

Figure 2. Raw data for all participants as a function of sex, menstrual cycle, and menopause across the three studies. Data for total words (top panel), switches (centre panel) and mean cluster size (bottom panel) are plotted against age in years. (HEP = high estrogen phase; LEP = low estrogen phase; PRE/PERIMENO = pre- and perimenopause stage; POSTMENO = postmenopause stage).

Figure 2.



4 Discussion

4.1 Mean differences total words, switches, and mean cluster size

Among the group mean differences by sex, menstrual cycle, and menopause stage, only the contrasts between HEP and LEP women reached or neared statistical significance for the three dependent measures of verbal fluency. Indeed, the widest distinctions in performance and strategy measures occurred in the younger women as a function of their menstrual cycle phase, with women at HEP tending to produce more words as well as significantly more switches (as hypothesised) and larger clusters, than women at LEP. With the exception that younger women combined across cycle phases tended to produce fewer words than men, patterns of means for other comparisons, while not statistically significant, were generally in the predicted direction. Younger women tended to show more switches and larger cluster sizes than men, and pre/perimenopausal women tended to show more words, switches, and larger cluster sizes than postmenopausal women. Looking at the pattern of means from the four groups of women, those with higher within-study ovarian hormones (HEP and pre/perimenopausal groups) tended to produce the most words and used, or tended to use, the most switches. Although not specifically hypothesized, these groups also had or tended to have larger within-study cluster sizes compared to LEP and postmenopausal women.

Findings in this report are consistent with the mixed results reported in the literature on letter/phonemic based fluency, where advantages as a function of female sex, high menstrual cycle hormones, and pre-menopausal status were detected, but varied in size and statistical significance (Hirnstain et al. 2022; Hyde 2016; Sundström Poromaa and Gingnell 2014; Weber et al. 2014). Sex differences with women producing more spoken (Costa et al. 2014; Weiss et al. 2006) and written words than men (Scheuringer and Pletzer 2017) have been demonstrated in some, but not in all studies (Halari et al. 2005; Scheuringer et al. 2017; Sokołowski et al. 2020). The current results are also in accordance with previous research which attributed higher estrogen levels to the enhancement of performance in cognitive areas where females typically outperform males, such as fine motor and verbal abilities (Hampson 1990b, a; Hamson et al. 2016; Maki et al. 2002; Wadnerkar et al. 2006; Whiteside et al. 2004). Menstrual cycle effects with women at higher hormone phases showing better verbal fluency scores than at the lower hormone phase have been shown (Hampson 1990a). In a detailed analysis of narrative fluency, Schultheiss et al. (2021) found a more robust female advantage in age groups 9-17 and 18-50 years compared to children below 9 and adults over 50. Effect sizes were small to medium and strongest in the written modality. Thus, the impact of female reproductive hormones on linguistic fluency appears to be both task and life-stage specific. For example, in contrast to the current study's findings in spoken letter fluency, menstrual cycle effects were not significant for total words, switches or cluster size in written phonemic fluency (Scheuringer and Pletzer 2017). In relation to reproductive stage, and partly consistent with the current study's findings of non-significant decreases in letter fluency, lower phonemic fluency scores have been observed for total words in women after menopause in some (Berent-Spillson et al. 2012; Weber et al. 2014) but not all studies (Kilpi et al. 2020) or menopausal stage comparisons (Weber et al. 2014).

In relation to strategy use, Weiss et al. (2006) reported that women used more switches in a spoken phonemic fluency task, but Sokolowski et al. (2020) did not find a sex difference. For written phonemic fluency, results were variable and condition specific, with women using

1 more switches unless instructed to use clusters (Scheuringer and Pletzer 2017) but not
2 consistently so (Scheuringer et al. 2017), and not in a neutral version of the task (Scheuringer
3 et al. 2017). For cluster size, Weiss et al. (2006) reported that men used larger clusters than
4 women for spoken fluency, but this was not replicated in other reports of spoken (Sokołowski
5 et al. 2020) or instructed written verbal fluency (Scheuringer and Pletzer 2017).
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7 In the current study, as noted above, only the menstrual cycle comparisons yielded
8 statistically significant, or near-significant, mean differences for total words, mean cluster
9 size and number of switches. These results corresponded to medium effect sizes based on
10 Cohen's *d* values greater than 0.50 from post hoc mean comparisons and partial eta-squared
11 values greater than 0.0588 from between-group effects in the ANOVAs. However, the
12 between group comparisons with this sample of 35 women were powered at 80% only for
13 large effects. Despite this limitation, the finding of variation in women's verbal fluency as a
14 function of menstrual cycle phase explains in part the null findings when the data were
15 analysed by sex. The mean values for total words, switches and cluster size in men were
16 between (in terms of rank order) the higher mean values for HEP women and the lower mean
17 values for LEP women (Table 2). These findings, together with evidence from our previous
18 work in speech production and perception (XX 2004; XX 2006; 2008) indicates that sex
19 differences can be obscured by menstrual phase variation in women. This conceptual
20 framework is useful in part for understanding the nature of hormone related variability
21 underlying small effect sizes in sex differences from studies that do not systematically control
22 for menstrual phase. Our results also emphasize the need to study group differences in the
23 relationships between performance and strategy measures as an additional way to investigate
24 underlying cognitive processing differences in the context of sex and hormone-based factors.
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30 **4.2 Correlations between total words, switches and mean cluster size**

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33 Previous studies have shown significant correlations between the number of switches and
34 total words produced when looking at spoken phonemic verbal fluency (Troyer et al. 1997)
35 and its written counterpart task (Scheuringer et al. 2017). In relation to sex, effects have been
36 mixed. Weiss et al. (2006) showed the same pattern in male and female groups, with
37 significant correlations between switching and total words. However, Scheuringer et al.
38 (2017) showed that women had a larger magnitude of correlation between switches and total
39 words compared to men on written phonemic fluency, and that this distinction was more
40 prevalent under neutral (i.e., standard) and clustering-based instructions than under
41 switching-based instructions. Neither study showed any correlations for men or women
42 between total words and cluster size (Scheuringer et al. 2017; Weiss et al. 2006). Thus, our
43 findings, in relation to correlations between switches and total words in women compared to
44 men, are consistent with, and expand upon Scheuringer et al.'s (2017) results. In letter based
45 fluency, our correlation of 0.848 between total spoken words and switches in HEP women
46 (n=18) is consistent with Scheuringer et al.'s (2017) correlation of 0.82 between written
47 words and switches in women (n=19) who were tested during the luteal phase. Our results,
48 based on a design that specifically compares women at the HEP and LEP menstrual cycle
49 phases, adds an important within-sex comparison to this literature.
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55 The correlations between total words, switching and clustering that were statistically
56 significant, and/or representing large effect sizes, were compared. This was done to elucidate
57 patterns in relation to hormonally related effects on cognitive organisation above and beyond
58 those detected with standalone measures of word count, switches, and cluster size. Patterns of
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correlations emerged with recurring features across the five participant groups as a function of the intersections between sex and hormonal status.

First, switches correlated most highly with total word count in both groups of younger women, but to a lesser extent in both groups of older women and men. When organised by rank order of correlation between total words and number of switches, the degree to which switches correlated with total words followed a continuum consistent with ovarian hormone levels, from highest to lowest, starting with HEP women, followed by LEP women, then pre/perimenopausal women, and postmenopausal women; men had the lowest ranked correlation (Table 5). Compared to HEP women, correlations between total words and switches were significantly lower in the latter three groups. However, only the comparison of correlations between HEP and postmenopausal women withstood Bonferroni corrections.

Second, mean cluster size correlated most highly with total word count in LEP women, followed in rank order by men, postmenopausal women, pre/perimenopausal women, and HEP women (Table 4). The difference in correlations for total words and mean cluster size approached significance only in the comparison between LEP and HEP women (Table 4).

[insert Table 5 about here]

Table 5. Correlation analyses arranged by rank order of relationship magnitude between total words and switches with large effect sizes ($r > 0.5$) indicated in bold (Cohen 1992). Uncorrected p-values are presented (two-tailed significance $*p < 0.05$; $**p < 0.01$). Correlations that survived Bonferroni corrections for multiple comparisons $p < 0.05/5 = p < .01$ are underlined.

	Total words & switches	Total words & mean cluster size	Directional comparison of correlations with total words
HEP Women n=18	<u>0.848</u>** p<0.001	0.052 p=0.837	switches > cluster size
LEP Women n=17	0.577* p<0.015	<u>0.639</u>** p=0.006	switches < cluster size
Pre/Perimenopause Women n=19	0.437 p=0.061	0.431 p=0.065	switches = cluster size
Postmenopause Women n=52	<u>0.408</u>** p=0.003	<u>0.506</u>** p<0.001	switches < cluster size
Men n=20	0.400 p=0.080	<u>0.612</u>** p=0.004	switches < cluster size

Combining these two features resulted in three profiles (Table 5), whereby correlations with total words were either:

- (i) higher for switches, as in HEP women;
- (ii) equivalent for switches and cluster size, as in pre/perimenopausal women;
- (iii) or, higher for cluster size, as in LEP women, postmenopausal women, and men.

By framing these profiles in terms of sex by hormone interactions, some preliminary interpretations may be drawn. At the HEP of the menstrual cycle, women in their twenties used a switching strategy more than clustering to achieve their total number of words. In the years prior to and during the perimenopause, women in their late forties and early fifties, showed a blended profile of strategy use in achieving their total words. At the LEP of the menstrual cycle and after menopause, women at both life span stages applied clustering to a

greater extent than switching toward their total word performance – a pattern also observed for men in their twenties.

4.3 Combined means and correlations

Integration of the patterns of means and correlations was conducted to yield a cross-group synthesis of the findings. These descriptions are provided for conceptual purposes and are based on a combination of significant and non-significant mean differences and correlations. As such, they are exploratory in nature and are provided for the purpose of generating future research hypotheses. HEP women and pre/perimenopausal women had the highest word counts, alongside a pattern of associations where total words-to-switches were more highly or equally correlated in relation to total word-to-cluster size. In contrast, the three groups with the lowest word counts were those that showed higher total words-to-cluster size correlations compared with total word-to-switches correlations, i.e., LEP women, postmenopausal women, and men. It can also be hypothesised that women have a flexible range of strategies that are differentially deployed across hormone phases and stages throughout a woman's adult life span. The results observed within the younger women, as a function of menstrual phase, are consistent with a neurofunctional system capable of accessing different strategies during different neurophysiological states. This capacity for change in and of itself represents a capability to make use of a variety word finding strategies to complete the same task.

Effective patterns of cognitive switching at the menstrual HEP may be due in part to the activating effects of estrogen. The reduced number of switches in women at the LEP phase is consistent with findings in girls with Turner's syndrome who exhibited a reduced number of switches compared to healthy controls (Temple 2002). These results are also in line with previously reported facilitating effects of estrogen on executive function (Dunkin et al. 2005; Erickson et al. 2007; Keenan et al. 2001; Reuben et al. 2021; Sundström Poromaa and Gingnell 2014). Together the evidence suggests that elements of executive functioning may play a greater role in verbal fluency performance in adult women during higher hormone days of the menstrual cycle. The capacity for sex differences and menstrual cycle effects in strategy use has also been studied in spatial tasks, from which one may draw conceptual parallels to the verbal domain. Holden and Hampson (2021) found that women and men relied on different cue types in completing a spatial short term memory task. They also showed a correlation between circulating levels of estrogen and the degree of reliance on the favoured categorial cue type used by women. Analogies may also be drawn from spatial maze behaviour, where women integrated two types of cues compared to men who relied mainly on one cue type (Sandstrom et al. 1998). Thus, the current study's correlation patterns suggest that in letter based verbal fluency, total word counts in men are more closely linked to clustering, whereas total word counts in women may be associated with clustering and/or switching. During the cycle phases when estrogen is high, the neurocognitive mechanisms for deploying flexible switching strategies in verbal fluency may be mediated by ovarian hormone activation of prefrontal cortex.

Postmenopausal women in the current study showed a pattern of correlations similar to what was observed in LEP women, with greater magnitude in the correlation between total words and cluster size, compared to total words and switches. This finding further solidifies the interpretation above that the presence of high circulating levels of ovarian hormones, as observed for women in the HEP of the menstrual cycle, underpins select use of a switching-based strategy for retrieving more words in the verbal fluency task. Additional support for a

1 connection between estrogen and the capacity to deploy an effective switching strategy for
2 verbal fluency, comes from research in postmenopausal women. Switching in verbal fluency
3 involves the cognitive flexibility to break from existing sets, i.e., clusters, and generate word
4 strings with distinct letter patterns (e.g., breaking from the cluster /*split, splinter, splendid,*
5 *splash/* to produce the word string /*stick, sandal, stutter/*). Changes at menopause may be due
6 in part to reductions in estrogen's facilitative effects on prefrontal cortical systems involved
7 in regulating cognitive flexibility (Berent-Spillson et al. 2012; Kantarci et al. 2018; Vega et
8 al. 2016). Thus, as a core dimension of executive function (Diamond 2013), cognitive
9 flexibility measured by switching in verbal fluency, may be mediated by hormone
10 replacement therapy (HRT). Reports have shown that estrogen-based HRT is associated with
11 improved executive function measures (Dunkin et al. 2005; Keenan et al. 2001) and related
12 cognitive processes such as attention (Smith et al. 2001) and working memory (Duff and
13 Hampson 2000) in women after menopause (Navarro-Pardo et al. 2018). Indeed, Erickson et
14 al. (2007) found that up to 10 years of HRT use in postmenopausal women was associated
15 with fewer perseverative errors on the Wisconsin Card Sort Task and a lower degree of
16 volume loss in the prefrontal cortical grey matter.
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21 In pre/perimenopausal women, the correlation between total words and switches was similar
22 to those observed in postmenopausal women and men (Table 3). However, only in the
23 pre/perimenopause group was there near equivalence in the correlations for total words and
24 switches ($r=0.437$) compared to total words and cluster size ($r=0.431$). The idea that late
25 premenopause and perimenopause are part of a transitional stage to a more stable
26 postmenopausal neurocognitive state is supported by behavioural (Weber et al. 2014) and
27 neuroimaging studies (Mosconi et al. 2021). The current study's data indicate that
28 perimenopausal changes in letter fluency performance may reflect an underlying reduction in
29 cognitive access to patterns of strategy use available to women at the HEP in earlier
30 adulthood. This, in addition to subtle decreases in overall word finding performance, may
31 give rise to the psychological experience of word finding difficulty during menopausal
32 transition stages – even in instances when actual performance may have stabilised.
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36 We note some methodological limitations in interpreting our findings. One is the degree of
37 statistical power afforded by the sample sizes in each of the three group mean comparisons
38 (i.e., ANOVAs). The menopause comparisons were powered at 80% for both medium and
39 large effects. The sex difference and menstrual cycle comparisons were powered sufficiently
40 for large effects, which were consistently observed only for the within-subjects factor, letter,
41 in analyses of total words. Between group differences were observed in the menstrual cycle
42 comparison but at 12.6% (cluster size) and 12.7% (switches) were just below the threshold
43 required for large effects (Cohen 1977; Richardson 2011). Taking this into account, the data
44 analysis was conducted conservatively, using a collection of methods that comport with the
45 sample size, and which also control for the risk of type 1 errors, including: omnibus analyses
46 of variance as the basis for mean differences; statistical corrections for multiple post-hoc
47 comparisons of means and for multiple correlations; presentation of effect sizes for mean
48 difference effects and correlations; bootstrapped correlation computations presented with
49 confidence intervals; and supplemental non-parametric correlations.
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54 A second limitation is the lack of precise temporal response data to support a more granular
55 analysis of the timing of lexical access and word production in relation to clustering and
56 switching cognitive processes. Addressing these issues in future research would enable
57 confirmatory research on the potential distinctions in hormonally based comparisons – in
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1 particular, distinctions between of verbal cognition in women at lower hormone phases/stages
2 and men which are likely to have different neuropsychoenocrinological bases.

3 4 **4.4 Conclusions and Implications**

5 Verbal fluency demands speed and accuracy in generating words (Melinder et al. 2005). It
6 also requires organised and efficient word retrieval, where participants must monitor their
7 responses, providing appropriate words and inhibiting inappropriate ones (Azuma 2004;
8 Henry and Crawford 2004). There is a tendency to produce words in groups or clusters which
9 share a common property. When one cluster is exhausted participants may switch to another
10 (Azuma 2004; Hirshorn and Thompson-Schill 2006; Melinder et al. 2005; Troyer et al. 1997).
11 Results of this study, specifically the mean differences and the patterns of correlations
12 showing large effect sizes, suggest that the ability to produce clusters of words and make
13 switches between clusters in a letter-cued and timed spoken verbal task is impacted by
14 menstrual phases and menopausal stages in women.
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18 This unique study, combining results from a series of datasets, examined verbal fluency
19 performance, strategy use, and performance-strategy associations in healthy adults. Results
20 provide insight into the confluence of factors related to sex, menstrual cycle phase, and
21 menopausal stage that shape cognitive strategy. Moreover, the performance-strategy
22 correlations between total word count, switching and clustering highlighted distinctions that
23 have not been previously revealed through examination of verbal fluency word count alone.
24 From a neuropsychological perspective, the patterns of correlations between total words and
25 switching provide an indirect measure of the close interplay between estrogen levels and
26 verbal thought processes in women across menstrual phases in early adulthood, and
27 menopausal stages in mid and later life. The cross-sectional nature of the studies limits
28 definitive conclusions about cause-effect relationships yet provides insight into the dynamic
29 and complex interplay of sex differences, hormone effects, and reproductive life stages
30 studied here. Further research will be required to more precisely characterise the hormonally
31 mediated neurocognitive mechanisms that influence switching and clustering strategy use in
32 verbal fluency.
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37 On the government, employment, and workplace policy front, there is a growing
38 acknowledgement of the socioeconomic and occupational impact of the menstrual cycle and
39 menopause (GOV_UK 2017; Griffiths et al. 2010; Riach and Jack 2021; Whiteley et al.
40 2013). There is also increasing clinical interest in understanding issues such as the impact of
41 the menstrual cycle on mental health (Jang and Elfenbein 2019) and of menopause and
42 estrogen exposure on cognitive wellbeing in later life, particularly in the context of aging,
43 acquired and progressive neurological conditions such as dementia (Gurvich et al. 2018; Jett
44 et al. 2022; Paganini-Hill et al. 2020; Rahman et al. 2019; Ryan et al. 2009; Taylor et al.
45 2019). Indeed, there is an urgency to understand the impact of menopause on women's health
46 with global rises in people over 60 years of age (Jett et al. 2022; Nebel et al. 2018; UN 2020;
47 WHO 1996). These applied spheres of social and biomedical activity heighten the need for
48 research designed to generate new knowledge on how sex, hormones, and related
49 reproductive factors shape human neurocognitive profiles in people of all ages. In this
50 context, the current study highlights the importance of looking beyond surface measures of
51 behavioural performance to more fully appreciate the variability in cognitive processes
52 employed by women at different phases of the menstrual cycle, stages of menopause, and
53 ages of adult life. Harnessing this variability is key to the design of neuropsychological
54 assessments, and ultimately to the development of policies and practices, that are sensitive
55 and responsive to the distinct cognitive profiles of women and men.
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Supplementary Material

Supplementary Table 1. Inter-rater reliability using Pearson's correlations (intraclass correlations coefficients in brackets) as a function of data source, letter or whole task, and dependent measure.

Study data source	Letter / Task	Total Words	Switches	Mean Cluster Size
First menstrual cycle and sex differences study, data compared for all N = 45 cases	F	0.990 (.99)	0.914 (.95)	0.940 (.96)
	A	0.987 (.99)	0.960 (.98)	0.929 (.96)
	S	0.974 (.99)	0.947 (.97)	0.890 (.94)
	FAS	0.990 (.99)	0.985 (.98)	0.945 (.96)
Second menstrual cycle study, data compared for n = 12 subsample of cases	F	0.987 (.98)	0.978 (.96)	0.980 (.97)
	A	0.996 (.99)	0.974 (.98)	0.904 (.88)
	S	0.989 (.99)	0.997 (.99)	0.786 (.76)
	FAS	0.997 (.99)	0.975 (.97)	0.933 (.89)
Menopause stage study, data compared for n = 8 subsample of cases	F	0.990 (.99)	0.980 (.98)	0.937 (.94)
	A	0.943 (.94)	1.000 (1.00)	1.000 (1.00)
	S	0.980 (.98)	0.872 (.88)	0.976 (.98)
	FAS	0.979 (.98)	0.980 (.98)	0.979 (.98)

Supplementary power estimate calculations.

Sex differences: Estimates of sample size to achieve 80% statistical power for medium effect sizes ($f = 0.25$ $\eta_p^2 > 0.0588$) in repeated measures ANOVAs ($\alpha = 0.05$, $k = 2$, repeated measures = 3, median correlation among repeated measures = 0.330, and median epsilon = 0.976) was $N=72$ for between factor effects and $N=38$ for within factor effects and interactions of within and between factors. An $N=20$ for between factor effects and $N=12$ for within factor effects and interactions of within and between factors would be required to achieve 80% power for large effects sizes ($f = 0.40$ $\eta_p^2 > 0.1379$).

Menstrual cycle phase: Estimates of sample size to achieve 80% statistical power for medium effect sizes ($f = 0.25$ $\eta_p^2 > 0.0588$) in repeated measures ANOVAs ($\alpha = 0.05$, $k = 2$, repeated measures = 3, median correlation among repeated measures = 0.332, and median epsilon = 0.996) was $N=72$ for between factor effects and $N=36$ for within factor effects and interactions of within and between factors. An $N=26$ for between factor effects and $N=16$ for within factor effects and interactions of within and between factors would be required to achieve 80% power for large effects sizes ($f = 0.40$ $\eta_p^2 > 0.1379$).

Menopause stage: Estimates of sample size to achieve 80% statistical power for medium effect sizes ($f = 0.25$ $\eta_p^2 > 0.0588$) in repeated measures ANOVAs ($\alpha = 0.05$, $k = 2$, repeated measures = 3, median correlation among repeated measures = 0.226, and median epsilon = 0.998) was $N=64$ for between factor effects and $N=42$ for within factor effects and interactions of within and between factors. An $N=26$ for between factor effects and $N=18$ for within factor effects and interactions of within and between factors would be required to achieve 80% power for large effects sizes ($f = 0.40$ $\eta_p^2 > 0.1379$).

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Comments from Reviewer 1 in italics.

We appreciate the opportunity to further revise our paper. We have incorporated amendments in response to Reviewer 1 into the revised manuscript. Our responses and changes to the manuscript are detailed below (*reviewer comments are in italics*). Relevant sections are highlighted in the manuscript. Other minor editing corrections are also highlighted in the manuscript.

Reviewer #1:

OVERALL

This is the revised version of a manuscript entitled: "Cognitive strategy in verbal fluency: Sex differences, menstrual cycle, and menopause effects"

Sex, menstrual cycle phase, and menopause stage were used as covariates to explain total words produced, plus switching and clustering strategy. These were found not to differ greatly between groups. Correlations between total word performance and strategy measures were observed and these differed across groups. The authors argue that the study supports the idea that hormones and sex influences strategy use in verbal fluency.

Reading the manuscript for the 2nd time, I still don't really understand what all the analyses are supposed to show, unless to support the idea is that women's ability to think changes as a function of their menstrual cycle. Personally, I don't think this is the case, and I would definitely never write a paper on it unless I had an extremely strong case. But that is just me.

Having this suspicion after my first reading, I asked the authors to provide a theory which could explain the hypotheses and findings they report. The authors do their best to avoid this, but on p.6 they actually state that the study aims to provide "evidence for the role of ovarian hormones in women's executive function."

The paper addresses the theoretical explanation for the hypotheses and findings. The theoretical underpinnings of the paper were derived from well-established evidence bases showing sex, menstrual cycle and menopause effects on brain, behaviour and cognition (i.e., the literatures on hormone effects in non-human brain and behaviour; human sex differences in brain, behaviour-cognition; human menstrual cycle and non-human estrous cycle effects; human menopause effects). In the revised manuscript submitted in October 2024, citations to this wider literature were expanded throughout the Introduction [pages 3-6] and Discussion [pages 20-25]; these two sections also included numerous references from our research group, spanning over two decades of published work in the field of sex differences, menstrual cycle effects, and menopause effects on speech, language and related cognition.

To address the Reviewer's most recent comments, we have further supplemented the Introduction with: (i) a systematic review (Dubol et al., 2021 on page 3.) presenting evidence across 77 studies for menstrual cycle mediated effects in brain structure, chemistry and function, which influence affective and cognitive processing that includes verbal fluency and executive control; (ii) a systematic review presenting evidence from 82 studies for estrogen

mediated effects on human brain networks that includes studies of verbal fluency and executive function/control (Ruehr et al., 2024, on page 3).

Regarding more specific theory and evidence for hormone effects and executive function, in the revised manuscript submitted in October 2024, our aims, hypotheses, and theoretical rationale were explicitly presented in the Introduction [see page 6, last paragraph of Introduction]. Our positioning of the study's findings within the literature, and our interpretation of the study's findings are also explicitly presented in the Discussion [see page 23, paragraph 2; page 24, paragraph 1].

To summarise, our theoretical premise (general background and specific background to the study's focus), hypotheses, and research findings are in line with a growing volume of evidence that human brain and cognition are shaped by reproductive hormones.

If you actually think it is true that women's executive functions change over their period, and that this study shows it, then you should by all means write it. But if there are any women among the authors, I want you to consider what this statement implies and make sure that you consider its dangerous interpretations and troubling historical roots.

If this study is published, all co-authors can be said to be advocates of this viewpoint. If the results were strong and reproducible, then of course this would be important knowledge to disseminate. But do you honestly think this is the case or are you just looking to get a publication?

The authors are all women and have worked together on programmes of research in the area of sex differences, hormone-related effects, and reproductive life stage effects in relation to speech and language for over two decades. In addition, all the authors work in health-based academic and/or clinical contexts. These backgrounds afford the authors perspective, understanding, and commitment to conducting sound research in these areas with applications to human health and wellbeing.

The purpose of our research is to better understand how hormones shape neurocognitive aspects of verbal ability across the lifespan to provide clearer understanding of both common and divergent aspects of men's and women's cognitive and communicative profiles. Reviewer 1 is concerned mainly with the menstrual cycle findings of the current study; however, the menstrual cycle findings are consistent with the study's pattern of findings on sex differences and menopause effects.

Conclusions page 25. Findings unique to women (compared to men and compared between women at distinct hormone phases or reproductive stages) may inform research, policy and practice in relation to improving women's health and wellbeing (e.g., providing a healthy baseline for comparison to conditions involving brain injury and disease) - this argument forms the basis of the final section of our Conclusions. Indeed, there is an urgency to understand the impact of menopause on women's health with global rises in people over 60 years of age - we elaborate on this in the revised manuscript (Conclusions page 25), supported by two review articles and two global reports (Jett et al. 2022; Nebel et al., 2018; WHO, 1996; UN Dept of Economic and Social Affairs, 2020). Work to understand adult sex differences and menstrual cycle effects in younger adults is a central part of the evidence

base that informs research on menopause and hormonally based neurocognitive factors linked to dementia risk which is now emphasised in the Conclusions.

We are aware that any scientific finding can potentially be used by others for positive or negative purposes. However, we also note the widespread advocacy in recent decades to include women in research and to understand the intersectionality of sex and gender with factors such as age and reproductive status (e.g., Society for Women's Health Research, <https://swhr.org/>; Organisation for the Study of Sex Differences, <https://www.ossdweb.org/>). In this context, the view that difference does not imply deficiency is central and underpins recent shifts in biomedical research towards incorporating knowledge about the physical and behavioural systems responsive to reproductive hormone variations approaches into precision medicine, customised for women. We make this point in the paper's final statement.

In my reading, the revised manuscript and the responses to my initial reading suggest the latter. To me this looks like a bunch of old data thrown together and then analysed to death. If I cared more, I would count all the statistical tests conducted in this paper to find out just how many one would expect to be significant by chance with an $\alpha=0.05$. But I will leave that to you.

I will not prevent you from stepping into the trap that you have set for yourselves. I just want you to do it with open eyes.

Below are the comments that I wrote while reading, before I gave up. Do with them what you please.

Our research councils advocate and fund research that makes novel use of existing data. Indeed, one of the grants that funded the current study was for that purpose - to build an archive designed to provide more powerful data analysis. The data in the current study represent a series of studies that were purposefully combined to shed light on reproductive hormone effects on cognitive processes in verbal fluency across the adult life course.

The data analysis was conducted conservatively using a collection of methods that comport with the sample size, and control for type 1 errors, including: omnibus analyses of variance; statistical corrections for multiple post-hoc comparisons of means and correlations; presentation of effect sizes; correlation computations with bootstrapping presented with confidence intervals; and supplemental non-parametric correlations. These have all been described/discussed in the paper.

Discussion Page 23. On the whole, we have applied a combination of standard practices in the bio-behavioural sciences for quantitative data analysis. Thus, it would be beyond the scope of this paper and the journal to further explain each one and its rationale in detail. We have summarised the conservative approach in terms of mitigating some of the study's limitations related to sample size.

DETAILS

Abstract:

Please add to the abstract for clarity: "The study found no direct effects of sex on verbal fluency, neither total words, mean cluster size or number of cluster switches."

This sentence has been amended accordingly.

P.6..L16. "This hypothesis was based on growing evidence for the role of ovarian hormones in women's executive function" See above.

We have responded to this above.

P.7.L16&20: "were not previously published in their entirety." -> "... entirety"

Page 7. We have amended these typos.

P.11. On power analysis. The authors have now removed the two words "A priori" from their description, which is good, I guess, but makes you wonder how they got there in the first place.

In their response to my first review, the authors write: "our original longitudinal studies were powered mainly to detect repeated measures effects across the menstrual cycle within women, in the domains of speech production and speech perception. For those measures of interest, medium effect sizes were estimated from existing two-phase menstrual cycle data for the acoustic phonetic measure of voice onset time, and for dichotic listening speech perception scores. We decided to publish the larger combined sample for verbal fluency data in the current paper precisely to enable larger data sets for this cross-sectional element of the menstrual cycle comparison. Moreover, it was decided to publish the data from the younger participants together with the data from the older women in order to further expand the size of the overall data set and its representation across the reproductive lifespan. Thus, we conducted the power analysis for the current study after joining the two smaller datasets for the younger participant groups. These power analyses were therefore conducted prior to the combined data analysis, but were not prior to the study design for the reasons outlined above. Conducting power analyses for the ANOVAs, together with the reporting of partial eta squared scores from the ANOVA effects, provides the statistical information needed to understand the current results in the context of type II ($\beta=0.20$) and type I ($\alpha=0.05$) error probabilities. For consistency and internal comparison purposes, this approach was applied to the menopause dataset. "

I would like the authors to add this paragraph to the methods section for transparency about why the manuscript includes a post hoc power analysis on cross-sectional data assumes large effect sizes for repeated measures. If I have misunderstood something, please explain your procedure in more details, but remember to do so in the manuscript. The reviewer is the future reader's representative, and I am sure that future readers will wonder how this all came together, as I did.

Methods page 11. The paragraph has been added to the methods. It has been edited to fit within this section of the manuscript.

“The original studies of younger adults were powered mainly to detect repeated measures effects across the menstrual cycle within women in the domains of speech production and speech perception. For those measures of interest, medium effect sizes were estimated from existing two-phase menstrual cycle data for the acoustic phonetic measure of voice onset time, and for dichotic listening speech perception scores. The decision to pool the data to achieve a larger combined sample for verbal fluency analysis in the current paper was taken to enable larger datasets for a cross-sectional menstrual cycle comparison. Moreover, it was decided to publish the data from the younger participants together with the data from the older pre/peri- and post menopause women to further expand the size of the overall data set and its representation across the reproductive lifespan. Thus, the power analysis for the current study was conducted after joining the smaller datasets from the younger participant groups. These power analyses (presented below) were therefore conducted prior to the combined data analysis, not prior to the study design, for the reasons outlined above. Conducting power analyses for the ANOVAs, together with the reporting of partial eta squared scores from the ANOVA effects, provides the statistical information needed to understand the current results in the context of type II ($\beta=0.20$) and type I ($\alpha=0.05$) error probabilities. For consistency and internal comparison purposes, this approach was applied to the menopause dataset.”

P. 12.L16. " all of which withstood Bonferroni adjustment ". This is ambiguous. Please rephrase to something like. "Post-hoc t-tests were Bonferroni-corrected for multiple corrections" so as to show that the other effects were not considered multiple tests.

Please make similar clarifications throughout the results section where the use of "all" can be misunderstood.

Pages 12-13 & 15-16. The text has been edited to signpost the post-hoc tests and describe the results adjusted for multiple comparisons.

P. 12.L21. Some nonsignificant effects are denoted "n.s." while others get an actual p-value. Be consistent, either one or the other.

Page 12-13 & 15-16. All instances where p-values were provided for non-significant effects have been amended to n.s.

P. 12.L48. "Group approached significance" Please rephrase to "There was no is significant effect of Group" .

Page 13. This has been amended. Similarly, the mention of a trend for a non-significant difference in the correlations between Total Words and Cluster size in HEP women and men was also deleted from the correlation analysis in section 3.1.2.

Please. Put results in the same order for ease of reading. You are reporting so many tests that it is very difficult to keep track of. Keeping the same order will make it easier.

Pages 12-13 & 15-16. The text has been edited so that all ANOVAs report the results in the order of Letter, then Group, and then Letter x Group effects.

Pages 15-16. The labelling for the Group factor in the Menopause results has been amended to be consistent with that used for Sex and Menstrual cycle ANOVA results.