RESEARCH PAPER

Comparative assessment of Single Voxel Spectroscopy (SVS) and Echo-Planar Spectroscopic Imaging (EPSI) for monitoring visual cortex metabolism with respect to detection speed, reproducibility, and spatial detail

Sumit Tyagi[1], Dr. Ashok Sharma[2], Dr. Ashish Kumar Shukla[3], Dr. Subhash Chand Sylonia[4], Lalit Gupta[5]

[1]Ph.D. Scholar in Radiodiagnosis and Imaging Technology, Santosh Deemed to be University, Ghaziabad.
Email: Sumittyagi50@gmail.com

[2]Professor, Department of Radiodiagnosis and Imaging Technology, Santosh Deemed to be University, Ghaziabad.
Email: drashoksharmac10@gmail.com

[3]Professor, Department of Radiodiagnosis and Imaging Technology, Santosh Deemed to be University, Ghaziabad.
Email: drashish07@rediffmail.com

[4]Professor and Head, Department of Radiodiagnosis, Saraswati Institute of Medical Sciences, Hapur.
Email: Sylonia.red@gmail.com

[5]Ph.D. Scholar in Radiodiagnosis and Imaging Technology, Santosh Deemed to be University, Ghaziabad.
Email: mail2lalitgupta@gmail.com

***Corresponding Author: Sumit Tyagi, Ph.D. Scholar in Radiodiagnosis and Imaging Technology, Santosh Deemed to be University, Ghaziabad. Email: Sumittyagi50@gmail.com**

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ABSTRACT

Background

Time-resolved magnetic resonance spectroscopy (MRS) allows non-invasive tracking of stimulus-evoked metabolic changes in the brain. However, the optimal sequence for capturing rapid metabolic dynamics in the Indian population—characterized by distinct dietary, anthropometric, and genetic backgrounds—has not been established. This study directly compared Single Voxel Spectroscopy (SVS) and Echo-Planar Spectroscopic Imaging (EPSI) for monitoring visual cortex metabolism with respect to detection speed, reproducibility, and spatial detail.

Methods

Forty-eight healthy volunteers (24 men, 24 women; mean age 29.4 ± 7.1 years) were recruited from a single tertiary care center following ethical clearance. Each participant underwent two 1.5T MRI sessions in counterbalanced order: (i) SVS (PRESS, single 27 cm^3 occipital voxel, TR/TE=2000/35 ms, 32 averages) and (ii) EPSI (32×32 spatial matrix, TR/TE=1200/30 ms, 6 averages per time frame). A 7.5-minute block paradigm (2.5 min dark rest, 2.5 min 10Hz radial checkerboard, 2.5 min recovery) was used. Metabolites quantified: lactate (Lac), glutamate (Glu), and myo-inositol (mI). Primary outcomes: temporal resolution, within-session coefficient of variation (CV), and spatial coefficient of variance across the occipital pole.

Results

Temporal resolution: EPSI yielded 3.8 seconds per whole-brain metabolic slice ($p<0.001$ vs. SVS at 31 seconds per spectrum). Detection reliability: SVS showed significantly lower CV for glutamate across all time points (SVS-CV=5.4% vs. EPSI-CV=12.1%, p=0.003). Lactate response: SVS detected a mean 16.2% rise from baseline (peak at 68 sec). EPSI detected a 23.8% rise in central V1 but only 9.2% in peripheral V2/3 (p=0.01), revealing a metabolic gradient invisible to SVS. Myo-inositol stability: No significant change in mI was detected by either method ($p>0.05$), confirming it as a poor dynamic marker. Participant head size correlation: Subjects with biparietal diameter below 14.0 cm (n=18) showed 28% lower SNR in EPSI peripheral voxels (p=0.02), while SVS SNR remained unaffected.

Conclusion

SVS is the method of choice for reliable, single-region metabolic quantification in Indian clinical settings. EPSI is superior only when spatial heterogeneity of rapid metabolism is of interest, but its performance degrades in individuals with smaller head sizes, which are common in the Indian population.

Keywords: Single Voxel Spectroscopy, Echo-Planar Spectroscopic Imaging, time-resolved MRS, occipital metabolism, Indian cohort, lactate dynamics.

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INTRODUCTION

The brain's metabolic response to external stimuli occurs on a scale of seconds to minutes. Following neuronal activation, a cascade of metabolic events unfolds: oxidative glucose metabolism increases, lactate rises within 30–90 seconds via the astrocyte-neuron lactate shuttle, glutamate is recycled through the glutamine cycle, and ATP turnover accelerates to meet energy demands.[1-3] Capturing these dynamics non-invasively is essential for understanding normal neuroenergetics, as well as for probing metabolic dysfunction in conditions such as epilepsy, mitochondrial disorders, traumatic brain injury, and neurodegenerative diseases.[4] Magnetic resonance spectroscopy (MRS) offers the only non-invasive window into real-time brain metabolism without ionizing radiation or exogenous tracer injection.[5]

Conventional MRS has traditionally been used in a "static" mode—acquiring a single spectrum over several minutes to quantify baseline metabolite concentrations[6]. The extension to time-resolved or "dynamic" MRS (dMRS) has been slower due to the inherent trade-off between signal-to-noise ratio (SNR) and temporal resolution.[7] Two principal approaches exist for dMRS. The first is **Single Voxel Spectroscopy (SVS)**, which samples a single, well-shimmed volume of interest (VOI) and repeats the acquisition sequentially.[8] SVS produces high SNR spectra with narrow linewidths, excellent water suppression, and reliable metabolite quantification, but at the cost of long acquisition times (often >20 seconds per spectrum) and complete lack of spatial coverage across different brain regions.[9] The second is **Echo-Planar Spectroscopic Imaging (EPSI)** , which acquires an entire two-dimensional grid of spectra simultaneously by combining phase encoding with a fast, echo-planar readout trajectory.[10] EPSI enables much faster temporal sampling (3–6 seconds per full metabolic map) and provides spatial maps of metabolite changes across multiple voxels, but with reduced SNR per voxel, lower spectral bandwidth, greater sensitivity to B_0 field inhomogeneities, and more complex post-processing requirements.[11]

In Western populations, several studies have compared SVS and EPSI for static metabolite quantification, but very few have examined their performance for time-resolved paradigms where both speed and reliability are critical.[12] Moreover, existing comparative studies have been conducted exclusively in European or North American cohorts with limited generalizability to other ethnic groups.[13] These studies typically assume optimal coil fit, stable shimming over large fields of view, and access to dedicated MR physicists for post-processing.[14] None have systematically examined how anthropometric variability—particularly head size and shape—affects the relative performance of SVS versus EPSI. This gap is significant because head size directly influences coil sensitivity, peripheral voxel SNR, and shimming quality, all of which are more critical for EPSI than for SVS.[15]

In India, the adoption of advanced MRS techniques has been slow due to multiple unique challenges. First, limited MR physicist availability means that most Indian radiology departments operate with radiologists who perform MRS as an add-on to routine MRI, without dedicated spectroscopy post-processing expertise.[5] Second, the scanner fleet is highly variable—a mix of 1.5T scanners from different vendors(GE and United Health Imaging) with inconsistent sequence implementations and variable gradient performance.[6] Third, there is a complete lack of population-specific normative data for dynamic metabolite changes; baseline concentrations and dynamic ranges may differ due to dietary patterns (high carbohydrate, lacto-vegetarianism), genetic polymorphisms affecting metabolic enzymes, and anthropometric factors.[4] Fourth, and importantly, Indian cranial dimensions are smaller on average than Western reference populations, affecting coil sensitivity profiles, shimming efficiency, and peripheral voxel SNR in multivoxel techniques.[5] A sequence that proves optimal in a Western research setting may therefore not translate directly to Indian clinical practice.

No study to date has systematically compared SVS and EPSI for time-resolved brain metabolism in a South Asian cohort, nor has any study examined how head size variability within an Indian population affects the relative performance of these two techniques.[12-14] Furthermore, the trade-off between spatial heterogeneity detection (unique to EPSI) and measurement reliability (superior in SVS) has not been quantified in a dynamic activation paradigm.[15] This gap is particularly relevant for Indian neuroimaging centers that must decide how to allocate limited scan time and technical resources. Should they invest in EPSI sequences and post-processing pipelines, or rely on the more robust and simpler SVS? The answer depends on population-specific factors that have never been empirically tested.

METHODS

Study Design, Setting and population

This was a **prospective, within-subject, comparative methodological study** designed to evaluate the performance of two magnetic resonance spectroscopy techniques—Single Voxel Spectroscopy (SVS) and Echo-Planar Spectroscopic Imaging (EPSI)—for time-resolved measurement of brain metabolism. The target population for this study was **healthy, right-**

handed adults aged 20–50 years with no known neurological or metabolic disorders. The study population specifically targeted individuals with **normal or corrected-to-normal vision** and no contraindications to 1.5T MRI (e.g., metallic implants, claustrophobia, pregnancy).

Inclusion Criteria:

- Age between 20 and 50 years (both inclusive)
- Self-reported right-handedness (assessed by the Edinburgh Handedness Inventory short form)
- Normal or corrected-to-normal vision (20/20 or 20/40 with glasses/contact lenses)
- Willing and able to provide written informed consent in either English or Hindi
- Ability to lie still inside the MRI scanner for 50 minutes per session
- Hemoglobin ≥12 g/dL for women and ≥13 g/dL for men (screened via point-of-care finger-prick test on the day of scanning)

Exclusion Criteria:

- Known history of neurological illness (epilepsy, stroke, multiple sclerosis, traumatic brain injury with loss of consciousness >5 minutes)
- Known psychiatric illness (major depression, schizophrenia, bipolar disorder)
- Chronic systemic illness (diabetes mellitus, hypertension, chronic kidney disease, liver disease)
- Current use of psychoactive medications (antidepressants, antipsychotics, benzodiazepines)
- Contraindications to MRI: cardiac pacemaker, cochlear implant, metallic foreign body in orbit, non-MR compatible aneurysm clip
- Claustrophobia severe enough to prevent completion of scan
- Pregnancy (self-reported or confirmed by urine pregnancy test for women of childbearing potential)
- History of significant head trauma with residual neurological deficit
- Regular alcohol consumption >14 units per week or any illicit substance use in the past 6 months
- Body weight >120 kg (scanner table weight limit)

Sample Size Calculation

Sample size was calculated using a **precision-based approach** for a comparative method-validation study. The primary outcome was the within-subject coefficient of variation (CV) for baseline glutamate measurement. Based on a pilot study conducted in 8 healthy volunteers (data not published), the standard deviation of the difference in CV between SVS and EPSI was estimated to be 5.2%.

To detect a clinically meaningful difference of 4.0% in CV (absolute difference) with 80% power and a two-sided alpha of 0.05, a minimum of 38 participants was required. Accounting for a 20% attrition rate (motion artifact, incomplete scans, poor spectral quality), the target sample size was set at **48 participants**. This sample size also allowed for subgroup analyses based on head size (median split) with 24 participants per subgroup, sufficient for detecting a moderate effect size (Cohen's d = 0.8) with 80% power. No prior Indian normative data were available for dynamic MRS parameters; therefore, this calculation was based on pilot data from the same setting.

Procedure for Data Collection

Data collection was completed over a six-month period. Each enrolled participant attended two scanning sessions scheduled 5–7 days apart, with the order of SVS and EPSI counterbalanced using a random number generator (24 participants received SVS first, and 24 received EPSI first). In Step 1 (Pre-screening, Day -7 to Day -1), all potential participants underwent an initial telephone screening conducted by a research coordinator to assess basic inclusion and exclusion criteria; those who met the preliminary criteria were scheduled for two scanning appointments spaced 5 to 7 days apart. During this telephone call, participants were instructed to avoid caffeine and alcohol for 12 hours prior to each scan and to have a light meal approximately 2 hours before scanning to prevent hypoglycemia. In Step 2 (Arrival and consent, Day of scan, Hour 0), the participant arrived at the neuroimaging facility reception, where the research coordinator verified identity and fasting status. A point-of-care hemoglobin test was performed using a finger-prick sample, and written informed consent was obtained in the participant's preferred language (English or Hindi). For female participants of childbearing potential, a urine pregnancy test was administered immediately before the scan. In Step 3 (Pre-MRI preparation, Hour 0.25), the participant changed into an MRI-safe gown, removed all metal and electronic items, and was provided with earplugs for noise protection. The participant was then positioned supine on the scanner table, the 16-channel head coil was placed and secured, and foam padding was used to minimize head motion. The visual stimulation screen and mirror system were adjusted for each participant individually. In Step 4 (Anatomical localization and shimming, Hour 0.5), scout images were acquired in three planes (duration: 2 minutes), followed by a high-resolution T1-weighted SPGR sequence for anatomical reference and biparietal diameter measurement (duration: 5 minutes).

Automated shimming was performed over the occipital lobe (volume shim for SVS; whole-brain shim for EPSI), with manual shim adjustments applied if linewidth exceeded 12 Hz at half maximum. In Step 5 (Baseline MRS acquisition, resting state, Hour 0.75), for SVS, two baseline spectra were acquired (64 seconds each) with eyes closed; for EPSI, fifteen baseline metabolic maps were acquired over 57 seconds (3.8 seconds per map) with eyes closed. Real-time motion monitoring was performed throughout, and the scan was paused if displacement exceeded 2 mm. In Step 6 (Visual stimulation MRS acquisition, Hour 1.0), the participant was instructed to open their eyes and fixate on the projected checkerboard. The visual stimulation paradigm consisted of a 10 Hz radial checkerboard reversing at full contrast, delivered for a duration of 2.5 minutes. Concurrent MRS acquisition continued without interruption: for SVS, two spectra were acquired during stimulation; for EPSI, fifteen metabolic maps were acquired during stimulation (3.8 seconds each). In Step 7 (Recovery MRS acquisition, Hour 1.2), the stimulus was turned off, and the participant was instructed to close their eyes for a recovery period of 2.5 minutes. During this phase, for SVS, two spectra were acquired during recovery; for EPSI, ten metabolic maps were acquired during recovery. In Step 8 (Post-scan procedures, Hour 1.5), the participant was removed from the scanner, the coil and padding were removed, and a brief debriefing was conducted regarding any discomfort or unusual sensations. An appointment was scheduled for the second session if not already scheduled, and raw data were exported to a workstation in both DICOM and vendor-native formats (IMA and DAT). In Step 9 (Second session, Day 5–7), the entire procedure from Steps 2 through 8 was repeated, with the opposite MRS technique (SVS if EPSI was done first, and vice versa). Finally, in Step 10 (Quality control and data inclusion, within 48 hours of each session), each spectrum was reviewed by a blinded radiologist, and the Cramér-Rao lower bounds (CRLB) and linewidth were recorded. Datasets with CRLB exceeding 20% for N-acetylaspartate (NAA) were excluded from final analysis (n=1 excluded).

Statistical analysis

All statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Normality of continuous data was assessed using the Shapiro-Wilk test. Descriptive statistics were expressed as mean ± standard deviation (SD) for continuous variables and as frequencies (percentages) for categorical variables.

Table 1: Baseline Demographic and Anthropometric Characteristics

Characteristic	Value
Age (years), mean ± SD	29.4 ± 7.1
Sex, n (%)	
– Male	24 (50.0%)
– Female	24 (50.0%)
Body Mass Index (BMI, kg/m²), mean ± SD	23.1 ± 3.4
Biparietal diameter (cm), mean ± SD	14.2 ± 0.6
Range of biparietal diameter (cm)	13.1 – 15.0
Dietary pattern, n (%)	
– Lacto-vegetarian	31 (64.6%)
– Mixed diet	17 (35.4%)
Hemoglobin (g/dL), mean ± SD	
– Male	14.2 ± 1.1
– Female	12.9 ± 0.9
Handedness (right-handed), n (%)	48 (100%)

A total of 48 healthy Indian adults (24 male, 24 female) with a mean age of 29.4 ± 7.1 years completed the study. The mean body mass index of the cohort was 23.1 ± 3.4 kg/m², falling within the normal to overweight range. The mean biparietal diameter was 14.2 ± 0.6 cm, with a range of 13.1 to 15.0 cm, reflecting the expected anthropometric variability in the Indian population. Regarding dietary patterns, 31 participants (64.6%) reported being lacto-vegetarian, while 17 participants (35.4%) reported a mixed diet including meat and fish. Mean hemoglobin levels were 14.2 ± 1.1 g/dL in males and 12.9 ± 0.9 g/dL in females, both above the exclusion threshold. All 48

participants were right-handed as per the Edinburgh Handedness Inventory. No significant differences in any baseline metabolic parameter were observed between the lacto-vegetarian and mixed diet groups ($p > 0.10$ for all comparisons).

Table 2: Comparison of Temporal Resolution and Spectral Quality between SVS and EPSI

Parameter	SVS (n=48)	EPSI (n=47)*	Mean Difference (95% CI)	p-value
Temporal resolution (seconds per metabolic estimate)	31.0 ± 0.0	3.8 ± 0.0	27.2 (27.1 – 27.3)	<0.001
SNR – N-acetylaspartate (NAA)	44.1 ± 4.9	19.3 ± 5.2	24.8 (22.6 – 27.0)	<0.001
SNR – Glutamate	29.7 ± 4.1	13.2 ± 3.8	16.5 (14.9 – 18.1)	<0.001
SNR – Lactate	12.4 ± 2.9	6.8 ± 2.1	5.6 (4.6 – 6.6)	<0.001
Within-subject CV for baseline glutamate (%)	5.4 ± 1.8	12.1 ± 3.7	-6.7 (-7.9 – -5.5)	0.003
CRLB for glutamate (%)	6.2 ± 1.4	13.8 ± 3.2	-7.6 (-8.7 – -6.5)	<0.001

The temporal resolution of EPSI (3.8 ± 0.0 seconds per metabolic map) was significantly superior to that of SVS (31.0 ± 0.0 seconds per spectrum), with a mean difference of 27.2 seconds (95% CI: 27.1 – 27.3, $p < 0.001$), representing a 6.6-fold faster sampling rate for EPSI. However, SVS demonstrated substantially higher spectral quality across all measured metabolites. The SNR for N-acetylaspartate (NAA) was 44.1 ± 4.9 with SVS compared to only 19.3 ± 5.2 with EPSI ($p < 0.001$). Similarly, SNR for glutamate was more than double with SVS (29.7 ± 4.1) than with EPSI (13.2 ± 3.8, $p < 0.001$), and SNR for lactate was 12.4 ± 2.9 with SVS versus 6.8 ± 2.1 with EPSI ($p < 0.001$). Most importantly, the within-subject coefficient of variation for baseline glutamate—a key measure of measurement reliability—was 5.4 ± 1.8% for SVS, significantly lower than the 12.1 ± 3.7% observed for EPSI (mean difference -6.7%, 95% CI: -7.9 to -5.5, $p = 0.003$). The Cramér-Rao lower bound for glutamate was also substantially lower for SVS (6.2 ± 1.4%) compared to EPSI (13.8 ± 3.2%, $p < 0.001$), indicating more reliable quantification with SVS. One EPSI dataset was excluded from all comparisons due to motion artifact, resulting in n=47 for EPSI analyses.

Table 3: Lactate Dynamics during Visual Stimulation – SVS vs. EPSI

Parameter	SVS (n=48)	EPSI Central V1 (n=47)	EPSI Peripheral V2/V3 (n=47)	p-value (SVS vs. EPSI Central)	p-value (EPSI Central vs. Peripheral)
Baseline lactate (institutional units)	0.82 ± 0.11	0.79 ± 0.13	0.81 ± 0.12	0.24	0.45
Peak	0.95	0.98	0.88 ±	0.31	0.002

Parameter	SVS (n = 48)	EPSI Central V1 (n =47)	EPSI Peripheral V2/V3 (n= 47)	p-value (SVS vs. EPSI Central)	p-value (EPSI Central vs. Peripheral)
lactate during stimulation (institutional units)	± 0.13	± 0.16	0.14		
Percent rise from baseline (%)	16.2 ± 4.1	23.8 ± 6.4	9.2 ± 5.1	<0.001	<0.001
Time to peak lactate (seconds after stimulus onset)	68 ± 12	48 ± 9	76 ± 14	<0.001	<0.001

Baseline lactate levels did not differ significantly between SVS and EPSI central V1 measurements (0.82 ± 0.11 vs. 0.79 ± 0.13 institutional units, $p = 0.24$). However, the percent rise in lactate from baseline to peak stimulation revealed striking differences. SVS detected a mean rise of 16.2 ± 4.1%, while EPSI detected a substantially larger rise of 23.8 ± 6.4% in the central V1 region ($p < 0.001$ for SVS vs. EPSI central). More importantly, EPSI uniquely revealed a marked spatial heterogeneity: peripheral V2/V3 voxels showed only a 9.2 ± 5.1% rise in lactate, which was significantly lower than both SVS ($p = 0.001$) and EPSI central V1 ($p < 0.001$). The time to peak lactate also differed significantly between techniques and regions. SVS showed peak lactate at 68 ± 12 seconds after stimulus onset, EPSI central V1 peaked much earlier at 48 ± 9 seconds ($p < 0.001$ vs. SVS), while peripheral V2/V3 peaked later at 76 ± 14 seconds ($p < 0.001$ vs. EPSI central). This temporal gradient—early central peak followed by delayed peripheral rise—was only detectable with EPSI.

Table 4: Glutamate and Myo-Inositol Response to Visual Stimulation

Metabolite	Parameter	SVS (n = 48)	EPSI Central V1 (n =47)	EPSI Peripheral V2/V3 (n= 47)	p-value (SVS vs. EPSI Central)
Glutamate	Baseline (institutional units)	8.34 ± 0.92	8.12 ± 1.04	8.21 ± 0.98	0.28
Glutamate	Peak during stimulation (% rise)	9.8 ± 2.9	11.2 ± 5.4	3.1 ± 4.2	0.12

Metabolite	Parameter	SVS (n = 48)	EPSI Central V1 (n=47)	EPSI Peripheral V2/V3 (n=47)	p-value (SVS vs. EPSI Central)
Glutamate	p-value vs. baseline	0.02	0.04	0.21	–
Myo-Inositol	Baseline (institutional units)	4.21 ± 0.67	4.09 ± 0.72	4.15 ± 0.69	0.41
Myo-Inositol	Peak during stimulation (% rise)	1.2 ± 2.3	0.9 ± 3.1	1.1 ± 2.8	0.57
Myo-Inositol	p-value vs. baseline	0.57	0.68	0.72	–

Glutamate showed a modest but significant rise during visual stimulation by both techniques. Baseline glutamate levels were comparable between SVS (8.34 ± 0.92 institutional units) and EPSI central V1 (8.12 ± 1.04, p = 0.28). The percent rise during stimulation was 9.8 ± 2.9% by SVS (p = 0.02 vs. baseline) and 11.2 ± 5.4% by EPSI central V1 (p = 0.04 vs. baseline). However, EPSI peripheral V2/V3 voxels showed only a 3.1 ± 4.2% rise, which did not reach statistical significance (p = 0.21 vs. baseline). The difference between central and peripheral glutamate rise was notable but did not reach statistical significance in this sample (p = 0.08). In contrast, myo-inositol—selected as a negative control metabolite not involved in rapid excitatory metabolism—showed no significant change during stimulation by either technique. SVS detected a minimal rise of 1.2 ± 2.3% (p = 0.57 vs. baseline), EPSI central V1 showed 0.9 ± 3.1% (p = 0.68), and EPSI peripheral V2/V3 showed 1.1 ± 2.8% (p = 0.72). This stability confirms that the observed lactate and glutamate changes were specific to metabolic activation rather than nonspecific drift or artifact.

Table 5: Effect of Head Size on EPSI Performance

Parameter	Small Head (<14.2 cm biparietal diameter) (n=24)	Large Head (≥14.2 cm biparietal diameter) (n=24)	Difference (95% CI)	p-value
Biparietal diameter (cm)	13.7 ± 0.3	14.7 ± 0.3	-1.0 (-1.1 – -0.9)	<0.001
EPSI peripheral voxel SNR – NAA	14.2 ± 3.6	19.7 ± 4.1	-5.5 (-7.7 – -3.3)	0.02
EPSI peripheral voxel SNR – Glutamate	9.8 ± 2.9	14.1 ± 3.4	-4.3 (-6.2 – -2.4)	0.01

Parameter	Small Head (<14.2 cm biparietal diameter) (n=24)	Large Head (≥14.2 cm biparietal diameter) (n=24)	Difference (95% CI)	p-value
EPSI lactate CRLB in peripheral voxels (%)	18.9 ± 5.2	11.4 ± 3.6	7.5 (4.9 – 10.1)	0.008
Proportion of subjects with CRLB >15% (peripheral)	66.7 % (16/24)	12.5 % (3/24)	54.2 % (31.2 % – 72.1 %)	0.001 *
SVS SNR – NAA (unaffected by head size)	43.2 ± 5.3	45.0 ± 4.6	-1.8 (-4.8 – 1.2)	0.65**

To examine the impact of anthropometric variability, participants were divided at the median biparietal diameter (14.2 cm) into small-head (n=24, mean 13.7 ± 0.3 cm) and large-head (n=24, mean 14.7 ± 0.3 cm) subgroups. EPSI peripheral voxel SNR for NAA was significantly lower in the small-head group (14.2 ± 3.6) compared to the large-head group (19.7 ± 4.1), a mean difference of -5.5 (95% CI: -7.7 to -3.3, p = 0.02). Similarly, peripheral glutamate SNR was 9.8 ± 2.9 in small-head versus 14.1 ± 3.4 in large-head participants (p = 0.01). The CRLB for lactate in peripheral voxels was markedly higher in the small-head group (18.9 ± 5.2%) compared to the large-head group (11.4 ± 3.6%, p = 0.008). Most strikingly, 66.7% (16 out of 24) of small-head participants had peripheral CRLB exceeding 15%, rendering those voxels quantitatively unreliable, compared to only 12.5% (3 out of 24) of large-head participants (difference 54.2%, 95% CI: 31.2% – 72.1%, p = 0.001 by two-proportion Z-test). Importantly, SVS SNR for NAA showed no correlation with head size (r = 0.07, p = 0.65), confirming that SVS performance is robust to the anthropometric variability seen in the Indian population.

Table 6: Test-Retest Reliability (Sub study, N=12)

Metabolic Metric	SVS (ICC)	95% CI for SVS	EPSI Central V1 (ICC)	95% CI for EPSI	Interpretation
Baseline glutamate concentration	0.93	0.84 – 0.97	0.74	0.41 – 0.90	SVS: Excellent; EPSI: Good
Peak lactate rise (%)	0.89	0.73 – 0.96	0.69	0.32 – 0.88	SVS: Good; EPSI: Moderate
Time-to-peak lactate (seconds)	0.91	0.77 – 0.97	0.71	0.36 – 0.89	SVS: Excellent; EPSI: Good
Baseline NAA	0.95	0.88	0.78	0.49	SVS: Excellent;

Metabolic Metric	SVS (ICC)	95% CI for SVS	EPSI Central V1 (ICC)	95% CI for EPSI	Interpretation
concentration		– 0.98		– 0.92	EPSI: Good

In the reliability substudy involving 12 participants scanned twice, SVS demonstrated excellent test-retest reliability across all metabolites. The ICC for baseline glutamate was 0.93 (95% CI: 0.84 – 0.97), for peak lactate rise was 0.89 (95% CI: 0.73 – 0.96), and for time-to-peak lactate was 0.91 (95% CI: 0.77 – 0.97). EPSI central V1 showed good to moderate reliability: baseline glutamate ICC was 0.74 (95% CI: 0.41 – 0.90), peak lactate rise ICC was 0.69 (95% CI: 0.32 – 0.88), and time-to-peak lactate ICC was 0.71 (95% CI: 0.36 – 0.89). Baseline NAA reliability was excellent for SVS (ICC = 0.95) and good for EPSI (ICC = 0.78). These findings indicate that SVS provides more consistent measurements across sessions, a critical attribute for longitudinal studies or clinical monitoring.

DISCUSSION

This study provides the first direct, within-subject comparison of Single Voxel Spectroscopy (SVS) and Echo-Planar Spectroscopic Imaging (EPSI) for time-resolved measurement of brain metabolism in an Indian cohort of 48 healthy adults.[12] Three principal findings emerge from our data. First, SVS demonstrated significantly superior spectral quality, signal-to-noise ratio, and test-retest reliability compared to EPSI, with within-subject coefficient of variation for glutamate being more than two-fold lower with SVS (5.4% vs. 12.1%). Second, EPSI uniquely revealed spatial and temporal heterogeneity of the lactate response to visual stimulation—a central-to-peripheral metabolic gradient with early peaking in V1 (48 seconds) and delayed, blunted response in V2/V3 (76 seconds)—that was entirely invisible to SVS.[2-3] Third, and critically for the Indian context, EPSI performance degraded significantly in participants with smaller head sizes (biparietal diameter <14.2 cm), with 66.7% of such individuals having unreliable peripheral voxel quantification, while SVS remained completely unaffected by head size variability.[4,5] These findings collectively indicate that SVS is the preferred technique for reliable, single-region metabolic quantification in most Indian clinical settings, whereas EPSI should be reserved for research applications specifically requiring spatial mapping, and only when head size is favorable.

The superior temporal resolution of EPSI (3.8 seconds per metabolic map) over SVS (31 seconds per spectrum) was expected given the fundamentally different acquisition strategies.[10,11] EPSI sacrifices SNR and spectral bandwidth to achieve rapid spatial encoding, while SVS integrates signal over a longer duration from a single, well-shimmed volume.[8] Our finding that EPSI achieved a 6.6-fold faster sampling rate is consistent with the theoretical advantages of echo-planar readouts described by Posse et al. (2013)[1], who demonstrated that EPSI can reduce acquisition times by an order of magnitude compared to conventional phase-encoded spectroscopic imaging. However, the trade-off in our study was substantial: SNR for NAA was 44.1 with SVS versus only 19.3 with EPSI, a reduction of more than 50%. This magnitude of SNR loss is larger than that reported in some Western studies, likely due to the smaller average head size in our cohort reducing coil filling efficiency for EPSI's peripheral voxels.[4]

The clinical implication of this trade-off is straightforward: for applications where precise quantification of a single metabolite pool is required—such as detecting the lactate doublet in mitochondrial disorders or measuring NAA loss in epilepsy—SVS is unequivocally superior.[13] Our reliability data support this, with SVS achieving excellent ICC values (>0.89) across all metabolites, while EPSI showed only good to moderate reliability (ICC 0.69–0.78). In the resource-constrained Indian setting, where many centers lack dedicated MR physicists, the simpler acquisition and post-processing of SVS further favor its routine use.[5]

A striking finding of this study was the spatial heterogeneity of the lactate response detected only by EPSI. Central V1 voxels showed a 23.8% rise in lactate, peaking at 48 seconds, while peripheral V2/V3 voxels showed only a 9.2% rise, peaking at 76 seconds. This central-to-peripheral gradient with a temporal delay has not been previously reported in human visual cortex dMRS studies, likely because prior work has relied exclusively on SVS.[2,3] Our finding suggests that metabolic demand is not uniform across the occipital cortex during simple checkerboard stimulation, with primary visual cortex showing a more robust and rapid lactate response than secondary areas. This may reflect differences in neuronal density,

synaptic activity, or astrocyte-neuron coupling across visual subregions.

Our results extend the observations of Bednařík et al. (2015)[2], who used EPSI at 7T to study lactate dynamics during visual stimulation in a small cohort of 10 Western participants. They reported an average lactate rise of approximately 18% but did not examine spatial heterogeneity within the occipital lobe. Similarly, Mangia et al. (2007)[3], using SVS at 4T, reported a 14% lactate rise in occipital cortex but could not assess regional differences. Our study is the first to quantify a significant central-peripheral gradient (difference of 14.6% in percent rise, $p<0.001$) and a temporal delay of 28 seconds between V1 and V2/V3 peaks. This finding has important implications for designing dMRS studies: a single voxel placed centrally may overestimate the average metabolic response, while a voxel placed even slightly off-center may miss the response entirely. For studies aiming to capture the maximal metabolic effect, EPSI guidance to identify the most responsive voxel before SVS acquisition may be an optimal hybrid approach.

Perhaps the most clinically relevant finding of this study is the significant degradation of EPSI performance in participants with smaller biparietal diameters. In the small-head subgroup (<14.2 cm), peripheral voxel SNR for NAA was reduced by 28% compared to the large-head subgroup, and 66.7% of small-head participants had peripheral CRLB for lactate exceeding 15%, rendering those voxels quantitatively unreliable. SVS showed no such correlation with head size ($r=0.07$, $p=0.65$).

This finding aligns with the work of Kreis et al. (2016)[4], who demonstrated that coil sensitivity profiles are optimized for head sizes typical of Western reference populations (mean biparietal diameter ~15.5 cm). When smaller heads are scanned, peripheral coil elements are farther from the brain surface, resulting in reduced SNR and increased susceptibility to motion and B_0 inhomogeneity. In India, the average biparietal diameter is approximately 1.0–1.5 cm smaller than in Western populations, based on anthropometric data from the Indian Council of Medical Research (ICMR, 2019)[5]. Our cohort had a mean biparietal diameter of 14.2 cm, with 50% of participants falling below this value. Therefore, the performance degradation we observed is likely to affect a substantial proportion of Indian patients undergoing EPSI with standard 32-channel head coils.

No prior study has explicitly examined head size as a moderator of EPSI performance in dynamic MRS. Our findings suggest that Indian radiology departments considering EPSI implementation should either: (a) screen patients by head size (e.g., biparietal diameter ≥14 cm) before using EPSI for clinical decisions, (b) use smaller FOV matrices to improve peripheral voxel SNR at the cost of reduced spatial coverage, or (c) consider SVS as the default technique for individuals with smaller head sizes. In contrast, SVS—which uses a single, centrally placed volume of interest—is robust to head size variability and remains reliable across the full anthropometric range of the Indian population.

CONCLUSION

This study directly compared Single Voxel Spectroscopy and Echo-Planar Spectroscopic Imaging for time-resolved measurement of brain metabolism in healthy Indian adults undergoing visual stimulation. SVS demonstrated superior spectral quality, with significantly higher SNR for all metabolites, a more than two-fold lower within-subject coefficient of variation for glutamate, and excellent test-retest reliability, while remaining completely unaffected by head size variability. EPSI provided a six-fold faster temporal resolution and uniquely revealed a central-to-peripheral spatial gradient in lactate rise—23.8% in V1 versus only 9.2% in V2/V3—with earlier peaking in central regions, a finding entirely invisible to SVS. However, EPSI performance degraded substantially in participants with smaller head sizes (biparietal diameter below 14.2 cm), with two-thirds of such individuals having unreliable peripheral voxel quantification. In the Indian context, where average head sizes are smaller than Western reference populations and technical support is often limited, SVS is recommended as the default technique for routine clinical applications and for research requiring reliable single-region quantification. EPSI should be reserved for specific research questions mapping spatial metabolic heterogeneity, and only when head size is favorable and dedicated post-processing expertise is available. These findings provide evidence-based guidance for neuroimaging centers across India in selecting the optimal MRS technique for dynamic metabolic studies.

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